

REPUPLIC OF YEMEN
FACULTY OF MEDICINE AND HEALTH
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DEPARTMENT OF COMMUNITY MEDICINE



The Last Outbreak of Measles in Yemen 2023

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Acknowledgment

We praise Almighty Allah for his help and blessing to us for completing our scheduled research on last outbreak of measles in Yemen. We extend our gratitude and appreciation to **Prof. Ahmed Al Haddad**, Head of the Department of Community Medicine - Faculty of Medicine and Health Sciences - Sana'a University, the godfather from whom we derive our strength and passion. At the same time, we send our gratitude to **Dr. Aisha Al-Da'eri**, who was assistant and supportive. We also thank the General Administration for disease control and Epidemiological Surveillance for their cooperation and high-quality dealing.

Dedication

This scientific paper is dedicated: - To the soul of the deceased of science and homeland **Dr. Ammat-Allateef Abu Talib**, To the soul of our colleague **Sala Abdullateef Alsharafi**, May Allah mercy them, to our fathers and mothers, the mountains on which we are based, who are burning themselves for us. To our brothers and sisters in whom we get stronger with.

With gratitude,

Research members

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Abbreviations

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
ADEM	Acute Demyelinating Encephalomyelitis
AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
APME	Acute Postinfectious Measles Encephalomyelitis
AR	Attack Rate
ART	Antiretroviral Therapy
BCE	Before the Common Eradication
CART	Combined Antiretroviral Therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CNS	Central Nervous System
COR	Crude Odds Ratio
COVID19	Corona Virus Disease 2019
CP	Core Principle
CRS	Congenital Rubella Syndrome
CSF	Cerebrospinal Fluid
CSO	Civil Society Organization
CVDPV2	Vaccine Derived Poliovirus
DC	Dendritic Cell
DTP	Diphtheria-Tetanus-Pertussis Vaccine
EDEWS	Electronic Disease Early Warning System
EEG	Electroencephalogram
EMR	East Mediterranean Region
EPI	Expanded Program on Immunization
Gavi	Global Alliance for Vaccines and Immunization
GPW	General Program of Work
HCD	Human Centered Design

HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
IA	Immunization Agenda
ICT	Intra Cranial Tension
IDP	Internally displaced person
IG	Immunoglobulin
IL	Interleukin
IT	Information Technology
ITFDE	International Task Force for Disease Eradication
IU	International Unit
IVIG	Intravenous Immunoglobulin
MBP	Myelin Basic Protein
MCV1	First Dose of Measles Containing Vaccine
MCV2	Second Dose of Measles Containing Vaccine
MI4A	Market Information for Access to Vaccine
MIBE	Measles Inclusion Body Encephalitis
MMR	Measles-Mumps-Rubella
MMRV	Measles-Mumps-Rubella-Varicella
MOPHP	Ministry of Public Health and Population
MOSRP	Measles Outbreak Strategic Response Plan
MRI	Measles Rubella Initiative
MRSF	Measles and Rubella Strategic Framework
MRSP	Measles and Rubella Strategic Plan
MSP	Measles Surveillance System
MV	Measles Virus
OR	Odds Ratio
PFU	Plaque-Forming Units
PHC	Primary Health Care
PIE	Post Infectious Encephalitis
PIRI	Periodic Intensification of Routine Immunization
PME	Primary Measles Encephalitis

RNA	Ribonucleic Acid
RSV	Respiratory Syncytial Virus
SAGE	Strategic Advisory Group of Experts on Immunization
SDGs	Sustainable Development Goals
SIA	Supplementary Immunization Activity
SLAMF1	Signaling lymphocytic Activation Molecule Family 1
SP	Strategic Priority
SSPE	Subacute Sclerosing Panencephalitis
TIP	Tailoring Immunization Programs
TSS	Toxic Shock Syndrome
UHC	Universal Health Coverage
UN	United Nations
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organization
YEFTP	Yemen Field Epidemiology Training Program

CHAPTER 1

INTRODUCTION

Background

Measles is an acute, viral, infectious disease. References to measles can be found from as early as the 7th century. The disease was described by the Persian physician Rhazes in the 10th century as “more to be dreaded than smallpox.”

In 1846, Peter Panum described the incubation period of measles and lifelong immunity after recovery from the disease. John Enders and Thomas Chalmers Peebles isolated the virus in human and monkey kidney tissue culture in 1954. The first live, attenuated vaccine (Edmonston B strain) was licensed for use in the United States in 1963. In 1971, a combined measles, mumps, and rubella (MMR) vaccine was licensed for use in the United States. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed. ^[1]

Globally; Measles kills more children than any other vaccine-preventable disease. Before the widespread use of vaccine 90% of children had contracted measles by the age of 10 years ^[2]. In 1980s, before widespread vaccination, measles caused more than two million deaths each year. As a result of the global effort to eradicate the measles virus by vaccination, approximately 20 million measles deaths have been saved. Using an effective vaccine reduced the deaths number from 550,000 to 90,000 during 2000 to 2016, the majority from developing countries, which accounted for 5% of all under-five mortality ^[3]. In spite of the prevalence of the vaccine, the disease is still a serious problem with a high mortality (10%) with malnutrition being an important factor. In temperate zone most cases of measles occur during winter and early spring. The incidence of measles increases during dry seasons in tropical zones. In 2000, measles was estimated to cause approximately 31 to 39.9 million illnesses worldwide with an estimated 733,000 to 777,000 deaths, making it the fifth most common cause of death in children under 5 years of age. Of these cases and deaths an estimated of 96,000 deaths due to measles were accounted in Eastern Mediterranean Region. By 2008, measles deaths had decreased to 7000 deaths from 96,000 in 2000 a reduction of 93%. ^[4]

In the last few years, the COVID-19 pandemic has interrupted immunization services, health systems have been overwhelmed, and we are now seeing a resurgence of deadly diseases including measles. For many other diseases, the impact of these disruptions to immunization services will be felt for decades to come.

In 2020, 23 million children missed out on basic childhood vaccines through routine health services, the highest number since 2009 and 3.7 million more than in 2019.

The risk for large outbreaks has increased as communities relax social distancing practices and other preventive measures for COVID-19 implemented during the height of the pandemic. In addition, with millions of people being displaced due to conflicts and crises including in Ukraine, Yemen, Ethiopia, Somalia and Afghanistan, disruptions in routine immunization and COVID-19 vaccination services, lack of clean water and sanitation, and overcrowding increase the risk of vaccine-preventable disease outbreaks.

Almost 17,338 measles cases were reported worldwide in January and February 2022, compared to 9,665 during the first two months of 2021.

27 April 2022 – An increase in measles cases in January and February 2022 is a worrying sign of a heightened risk for the spread of vaccine-preventable diseases and could trigger larger outbreaks, particularly of measles affecting millions of children in 2022. ^[6]

Pandemic-related disruptions, increasing inequalities in access to vaccines, and the diversion of resources from routine immunization are leaving too many children without protection against measles and other vaccine-preventable diseases.

Table (1): *Top 5 countries with reported measles cases in the last 12 months, until April 2022.* ^[5]

Country	Reported Measles cases	Rate per million cases	First dose measles coverage (%), 2019 ^[2]	First dose measles coverage (%), 2020 ^[3]
Somalia	9,068	554	46	46
Yemen	3,629	119	67	68
Afghanistan	3,628	91	64	66
Nigeria	12341	58	54	54
Ethiopia	3039	26	60	58

Table (2): *Provisional data based on monthly data reported to WHO (Geneva) as of early August 2023.*

Rank	Country	Number of Cases
1	India**	57,550
2	Yemen	24,596
3	Pakistan	10,549
4	Indonesia	5,637
5	Ethiopia	4,836
6	Cameroon	4,745
7	Nigeria	4,385
8	Türkiye	2,901
9	Somalia	2,711
10	Democratic Republic of the Congo (DRC)***	2,511

Despite the number of measles cases reduced in The East Mediterranean Region (EMR) in the latest years, it's still a problem in the region. The number of reported suspected measles were 34,835 in 2015 and 28,225 in 2016 while the laboratory confirmed measles were 8853 in 2015 and 5201 cases in 2016. In 2016, measles incidence per 1000,000 populations was higher in Sudan (42.94), followed by Oman (34.66) and United Arab Emirates (23.92)

Collapse of the health system and destroying large number of health facilities due to the ongoing war in Yemen lead to a sharp decline in coverage of measles vaccination that poses a substantial threat to population health. Falls to around 41% coverage nationally by late 2015 have been reported, and to 64% during 2017 in all Yemeni governorates^[7]. The reported measles cases from

January to May 2018, a total of 4474 measles and 91 deaths were reported compared with 3529 measles and 8 deaths were reported through 2017^[8,9]. Many outbreaks were investigated in some governorates. Such as Hajjah governorate in 2012^[10], and Al Hudaydah governorate in 2014^[11], Al Jawf and Sa'adah governorates in March 2015^[12,13], Amran governorate in 2017^[14], and Shabwah government in May 2018. And in the last two to three years the number of measles cases reported are daunting. The number that has been recorded is more than 22,000 measles cases in 2022, including 161 deaths. In early 2023, cases have already spiked to 9,418, with 77 children dead^[15].

The increase in measles and rubella cases among children in Yemen this year is occurring within a context of economic decline and low incomes, displacement, and overcrowded living conditions in camps, coupled with an overwhelmed health system, low immunization rates, and a large number of children who remain unreachable through routine immunization interventions. According to the WHO- UNICEF National Immunization Coverage Estimate for 2022, 27 percent of children under one year of age in Yemen are unvaccinated for measles and rubella and have not met the minimal set of vaccines for measles and rubella and have not met the minimal set of vaccines for full protect.^[16]

Presented Statement:

The problem addressed in this research is the increase of reported cases of measles in this year and the associated risk factors that contribute in this outbreak as well as the primary reason for continuing high childhood measles mortality and morbidity.

WHO suggested outbreak case definitions

Case definitions for case finding

Suspected case:

An illness in a patient with fever and generalized maculopapular (non-vesicular) rash, or in a patient whom a health care worker suspects has measles.

Clinical measles case:

Any person in whom a clinician suspects measles infection; or

Any person with fever and maculopapular rash (i.e., non-vesicular) and:

- Cough, or
- Coryza (i.e., runny nose) or
- Conjunctivitis (i.e., red eyes)

Final case classifications:

Laboratory-confirmed measles case:

A suspected case of measles that has been confirmed positive by testing in a proficient laboratory, and vaccine-associated illness has been ruled out. ^[17]

Epidemiologically linked measles case:

A clinical case of measles that has not been confirmed by a laboratory, but was geographically and temporally related, with dates of rash onset occurring 7–21 days apart from a laboratory-confirmed case or another epidemiologically linked measles case.

Clinically compatible measles case:

A clinical case of measles, but no adequate clinical specimen was taken and the case has not been linked epidemiologically to a laboratory-confirmed or epidemiologically linked case of measles or other communicable disease.

Discarded case:

A suspected measles case that has been investigated and discarded as non-measles through:

- Negative laboratory testing in a proficient laboratory on an adequate specimen collected during the proper time after rash onset, or
- Epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is not measles; or
- Confirmation of another etiology; or failure to meet the clinically compatible measles case definition

• WHO other definitions:

Definition of measles outbreak:

Suspected measles outbreak:

Five or more measles cases (with dates of rash onset occurring 7–21 days apart) that are epidemiologically linked.

Laboratory-confirmed measles outbreak:

Two or more laboratory-confirmed measles cases that are temporally related (with dates of rash onset occurring 7–21 days apart) and epidemiologically or virologically linked, or both

Acute measles-related death:

A measles-related death is a death in an individual with confirmed (clinically, laboratory or epidemiologically) measles in which death occurs within 30 days of rash onset and is not due to other unrelated causes, e.g., a trauma. ^[18]

- **WHO Key facts**

- Measles is a highly contagious, serious airborne disease caused by a virus that can lead to severe complications and death.
- Measles vaccination averted 56 million deaths being between 2000 and 2021.
- Even though a safe and cost-effective vaccine is available, in 2021, there were an estimated 128,000 measles deaths globally, mostly among unvaccinated or under vaccinated children under the age of 5 years.
- In 2022, about 83% of the world's children received one dose of measles vaccine by their first birthday through routine health services – the lowest since 2008. ^[17]

- **Public health concern**

Measles spread worldwide from the Renaissance. Measles is a highly infectious human diseases caused by virus, and frequently results in widespread outbreaks ^[19, 20]. It is often characterized by high morbidity and mortality rates globally, particularly in African and other developing countries. Mortality from measles infection is often secondary to severe complications. Complications of measles include severe pneumonia, diarrhea, blindness, deafness and encephalitis. The disease can also lead to lifelong disabilities including brain damage, blindness. ^[21]

Measles is still one of leading causes of death among children globally.

Despite the number of measles cases reduced in The East Mediterranean Region (EMR) in the latest years, it's still a problem in the region ^[22], due to its high communicability, even a minor drop in immunization coverage can result in rapidly spreading outbreaks and re-establishment of endemic transmission, as noted in our country in the recent past. Unvaccinated children and young adults are at a higher risk of developing measles and they place vulnerable groups such as infants and persons with contraindications to immunization at risk. ^[23]

Nearly every measles infection results in well-recognized clinical disease. In non-immunized populations almost every child will get measles early in life. The universality of the disease in non-

immunized communities, particularly those in the developing world, has led to a more or less passive acceptance of measles as an unavoidable risk of early life. The clinical spectrum of measles ranges from a mild, self-limiting illness to a fatal disease. Conditions encountered mainly in the developing world, e.g., unfavorable nutrition, high risk of concurrent infection, and inadequate case management -- particularly at home -- favor the development of complications and adverse outcome. Conversely, good clinical management of an otherwise healthy child, a situation seen mostly in the developed world, greatly influences the course of the disease. Hence many in the medical profession believe that measles is a mild disease except among populations living under particularly unfavorable conditions. Measles vaccine is effective in preventing disease in the individual and in controlling it in the community if it is given at the critical age when maternal antibodies wane and the risk of natural infection increases sharply and if a high immunization rate is maintained in the target population. The experience with immunization, particularly in sub-Saharan Africa, is rewarding: mothers who had previously accepted measles as an unavoidable risk clamor for immunization of their children once its effectiveness has been demonstrated. No reason exists for measles to claim its present toll of morbidity and mortality. With extension of the Expanded Program on Immunization of the World Health Organization, the impact of measles should progressively decline. ^[24]

Measles remains a major public health concern, causing over 100,000 deaths per year worldwide. Today, the most affected continents remain Africa, South America and Asia. ^[25]

- **Objectives**

- Provide an in-depth understanding of the measles virus as a causative agent, encompassing its virology, mode of transmission, clinical manifestation and pathophysiology. Offer valuable insights into the epidemiology of measles in Yemen by exploring its historical background and presenting current statistical data.
- Enumerate several methods for eradicating measles worldwide and identify which ones are successful.
- Discuss their advantages and disadvantages, particularly those used in Yemen.
- Identify the global plan and steps taken towards eliminating the virus.
- Gather national data pertaining to measles prevalence and incidence, highlighting high-risk groups.
- Specify local challenges encountered during eradication efforts.

- Discuss the importance of vaccination in preventing measles outbreaks. This includes information on vaccine efficacy, safety, and accessibility.
- Analyze the impact of misinformation and vaccine hesitancy on measles eradication efforts. This includes identifying common myths and misconceptions about vaccines and providing evidence-based information to address them
- **Literature review:**
There are many studies stating the measles outbreaks, the associated risk factors that contribute to their emergence, and the possible factors that increase the morbidity and mortality through each of these outbreaks.

In Uganda 2017, a case control study was conducted to 38 case-patients. We re-cruited 34 of those case-patients aged ≥ 1 year to participate in the case-control study, case-patients and controls were comparable in mean age (6.0 years among case-patients vs. 5.9 years among controls) and sex distribution (41% of case-patients and 42% of controls were males). During the bivariate analysis, 44% of case-patients and 2.3% of controls had been hospitalized in the pediatric department of Lyantonde Hospital for non-measles conditions 7–21 days before case-patients' rash onset. Visiting any health facility 7–12 days before case-patient's rash onset was a significant risk factor. The study conclude that this measles outbreak was amplified through nosocomial transmission in the pediatric department in Lyantonde Hospital. ^[26]

In Uganda 2018, a case control study of 36 participants whom age is less than or equal to five years old," All 34 facility-based measles cases were documented to have had maculopapular rash, conjunctivitis, and cough. Also, the majority had fever (97%), coryza (94.1%), lymphadenopathy (76.5%), arthralgias (73.5%) and Koplik's Spots (91.2%) as documented in the clinical registers. Similar symptoms were reported among 36 community-based cases. Getting infected even after immunized, low measles vaccination coverage was identified as the principal risk factors for this outbreak. ^[27]

In Qufl Shamr, Hajja government, Yemen ,2012, WHO case definition were used. An active household search was done to identify the cases from May 4th to 28th where cases/guardians interviewed using standard form. Serum specimens were tested using measles IgM ELISA. Sixty cases fulfill the case definition with mean age of 6 and male to female ratio of 1:2. Common symptoms were fever (100%), rash (68%), difficulty breathing (32%) and diarrhea (30%). Hemorrhagic manifestation and mouth ulcers present in 20%. Measles IgM was positive in 12

cases. Vaccine coverage among confirmed cases was 5% compared to 46% among non-confirmed (P-value =0.0006). Seven deaths (71%) reported among under-five children with case fatality of 12%. All deaths were from Al-Holog village and unvaccinated. Out of seven deaths, four were epidemiologically linked to confirmed cases. The study has concluded that this outbreak is the first measles outbreak in Yemen with high fatality rate. All deaths were unvaccinated and most confirmed cases from area where no vaccination services or vitamin A. ^[10]

In Saada government, Yemen 2012, A study has conducted a retrospective case finding surveillance of measles cases reported in AL-Jamhory and AL Salam hospitals, and main district hospitals, health centers and private clinics in Saada governorate from 1 January 2012. A measles case was defined as a person having fever, rash, and one of the following: cough, or coryza, or conjunctivitis, a reside in Saada governorate. Of the 804 reported measles cases, 445 (55%) were males; 359 (45%) were females. One hundred twenty (15%) were laboratory confirmed and 684 (85%) were epidemiologically linked cases.

The age groups that were affected mostly were children 3-15 year of age (n=362, 45%) and ≤ 1 year old (n=345, 43%). Among the 362 children 3-15 year of age, 190(52%) were boys and 172 (48 %) were girls. The attack rate was $(804/219563=36.6\%)$. There were 505 hospitalizations and 15 deaths. The study has concluded that this outbreak was caused by an imported measles into the displaced population of children, whose parents had refused to have them vaccinated because of vaccine safety concerns. High vaccination levels in the surrounding governorates and low rates of vaccine failure averted an epidemic. ^[13]

CHAPTER 2

EPIDEMIOLOGY OF MEASLES

SECTION 1

Epidemiology and Statistics of Measles outbreak in Yemen

1.1 DEFINITION

- **Definition of measles:**

Measles is a highly infectious disease characterized by En-anthema (Koplik's spot) during the prodromal stage and Ex-anthema with profuse watering of the eye and nose. ^[28]

- **Definition of measles according to the WHO organization and CDC (center for diseases control and prevention):**

Measles also called rubeola, "10-day measles," or "red measles", is a highly contagious, serious airborne disease. It is one of the most contagious diseases humans have ever faced caused by a virus that can lead to severe complications.

Despite the availability of a safe and effective vaccine, measles remains an important cause of death among young children globally, and can also lead to serious adverse outcomes such as pneumonia, blindness and encephalitis, and even death.

- **Another definition for Measles:**

Measles is a highly contagious viral disease that is characterized by a prodromal illness of fever, cough, coryza, and conjunctivitis followed by the appearance of a generalized maculopapular rash. ^[29]

1.2 CAUSATIVE AGENT

Measles virus is a spherical, non-segmented, single-stranded, negative sense RNA virus and a member of the Morbillivirus genus in the family Paramyxoviridae. Although RNA viruses typically have high mutation rates, measles virus is considered to be an antigenically monotypic virus; i.e., the surface proteins responsible for inducing protective immunity have retained their antigenic structure across time and distance. The public health significance of this stability is that measles vaccines developed decades ago from a single strain of measles virus remain protective worldwide. Measles virus is killed by ultraviolet light and heat, and attenuated measles vaccine viruses retain these characteristics, necessitating a cold chain for vaccine transport and storage.^[29]

- **Epidemiological Overview**

Infection was common during childhood before the measles vaccine. The virus is spread through direct contact and the air, infecting the respiratory tract and spreading throughout the body. Measles is a human disease and does not occur in animals. There is no animal reservoir for the infection. The measles vaccine is considered a great investment in public health and has made measles rare in industrialized countries. However, it remains common in many developing countries due to the failure to deliver at least one dose of the vaccine to all infants. The virus cannot survive outside the human body and carrier are not known to occur. Measles is highly infectious during the prodromal period and at the time of eruption, but communicability declines rapidly after the appearance of the rash. Measles affects virtually everyone in infancy and childhood, mostly in developing countries with poor environmental conditions. It can also affect older children in developed countries. One attack of measles generally confers life-long immunity, and second attacks are rare. Infants are protected by maternal antibodies up to six months of age, and immunity after vaccination is solid and long-lasting. Measles epidemics are common during winter and early spring, and population density and movement affect epidemicity. The lower the socio-economic conditions, the lower the average age at which children are attacked.^[30]

• Structure

The virus is approximately 150-300 nm in diameter and has a spherical shape with a lipid enveloped that surrounds its nucleocapsid core. The virus has a pleomorphic structures and genome consisting of a single stranded –ve sense RNA, the genome is approximately 15.849 nucleotides. The genome encodes six structural proteins encode the nucleocapsid N, matrix M, phosphoprotein P, fusion protein F, hemagglutinin H and large polymerase L and two non- proteins B and C.

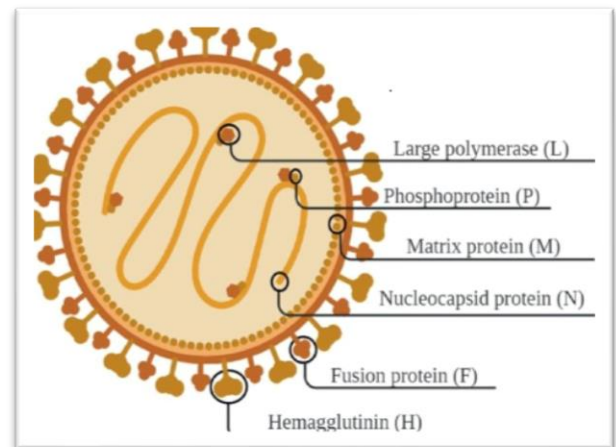


Figure (1): Structure of the Virus

The **P** protein of the measles virus interacts with the N protein and forms a complex with the viral RNA polymerase, which responsible for viral transcription and replication. The M protein is a transmembrane protein that interacts with the viral envelope and nucleocapsid core, it plays a critical role in viral assembly and budding by facilitating the transport of viral components to the plasma membrane and coordinating viral assembly at the plasma membrane. The F protein is a class I viral fusion protein that mediates viral entry into host cells, it interacts with the host cell receptor and undergoes conformational changes that facilitate viral fusion with the host cell membrane, leading to viral entry into the cytoplasm. The H protein is a viral attachment protein that binds to host cell receptors, initiating viral attachment and entry, the H protein interacts with the F protein and is responsible for the specificity of the viral attachment to host cells. The L protein is the viral RNA polymerase, which is responsible for viral transcription and replication, it interacts with the P protein and forms a complex with the viral RNA genome, which is essential for viral RNA synthesis.

There is only one antigenic type of measles virus. Although studies have documented antigenic changes in the H protein, these changes do not appear to be epidemiologically important (no change in vaccine efficacy has been observed).^[31]

1.3 PATHOPHYSIOLOGY

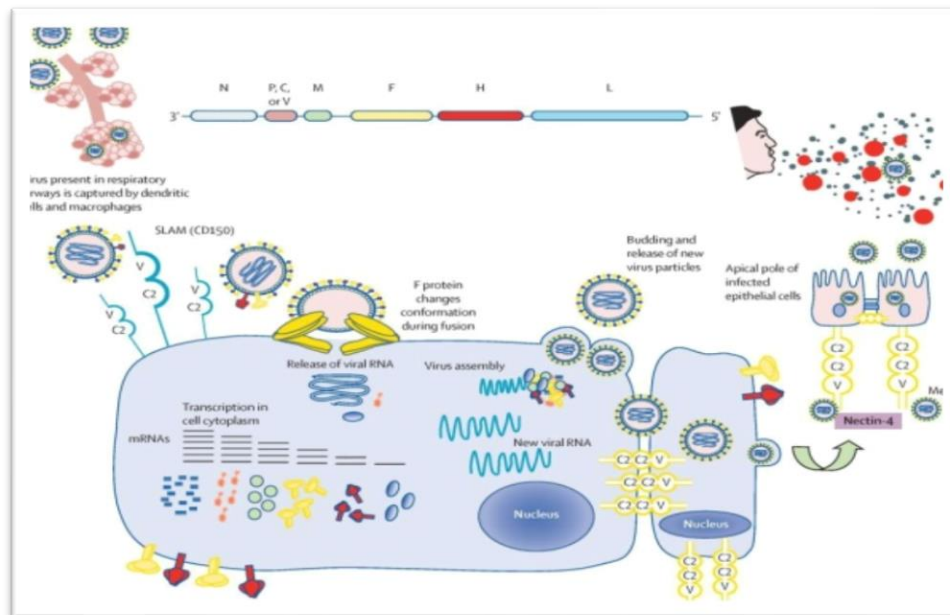


Figure (2): pathophysiology of the virus

- Measles is a systemic infection. Humans are the only natural hosts for measles virus, although numerous other species, including monkeys, dogs, and mice, can be experimentally infected.
- The virus gains access to the human body via the respiratory tract, where it multiplies locally; the infection then spreads to the regional lymphoid tissue, where further multiplication occurs.
- Primary viremia disseminates the virus, which then replicates in the reticuloendothelial system. Finally, a secondary viremia seeds the epithelial surfaces of the body, including the skin, respiratory tract, and conjunctiva, where focal replication occurs. ^[32]
- Measles is transmitted through respiratory inhalation and, after implantation of the virus in the upper respiratory tract, viral replication proceeds in the respiratory mucosal epithelium.
- The effect within individual respiratory cells is profound. Although measles does not directly restrict host cell metabolism, susceptible cells are damaged or destroyed by virtue of the intense viral replicative activity and the promotion of cell fusion with formation of syncytia. This results in disruption of the cellular cytoskeleton, chromosomal disorganization, and the appearance of inclusion bodies within the nucleus and cytoplasm. ^[33]

- Measles can replicate in certain lymphocytes; replication is followed by viremia and lymphatic dissemination which aids in dissemination throughout the body. Multinucleated giant cells with intranuclear inclusions are seen in lymphoid tissues throughout the body (lymph nodes, tonsils, appendix).
- After exposure, the virus multiplies in the respiratory tract epithelium (incubation period of 9-11 days, on average) and spreads to regional lymph nodes followed by viremia, which helps the virus to be transported throughout the body. Moreover, the virus is also shed in saliva and excreted in the urine. Koplik's spots appear on the tongue before appearance of rash on head, then trunk and other extremities. Humoral immune response plays an important role in clearing the virus from the hosts, with IgM appearing early in infection followed by IgG that persists for a long time. Cell-mediated immunity plays a role in disease progression.

- Post-infectious encephalitis and bacterial superinfections are major complications of measles virus infection. In some patients, there is a rare persistent infection of the CNS known as subacute sclerosing panencephalitis (SSPE).(figure 3) [33]

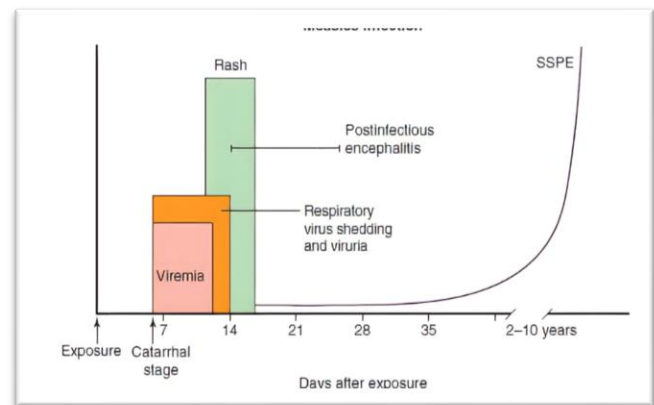


Figure (3): *Pathogenesis of measles virus*

- The viremia disappears, and the fever falls. The rash develops as a result of interaction of immune T cells with virus-infected cells in the small blood vessels and lasts about 1 week. (In patients with defective cell-mediated immunity, no rash develops.) Involvement of the central nervous system is common in measles.
- Symptomatic encephalitis develops in about one in 1000 cases. Because infectious virus is rarely recovered from the brain, it has been suggested that an autoimmune reaction is the mechanism responsible for this complication. In contrast, progressive measles inclusion body encephalitis may develop in patients with defective cell mediated immunity. Actively replicating virus is present in the brain in this usually fatal form of disease. [32]
- The virus can be demonstrated in the blood during the first week after illness onset, and viremia persists for up to 4 days after the appearance of rash. Viremia also allows the infection of conjunctiva, urinary tract, small blood vessels, and the CNS.

- During the viremia phase, measles virus infects T and B lymphocytes, circulating monocytes, and polymorphonuclear leukocytes without producing cytolysis. Profound depression of cell-mediated immunity occurs during the acute phase of illness and persists for several weeks thereafter. This is believed to be a result of virus-induced downregulation of interleukin-12 (IL 12) production by monocytes and macrophages. The effect on B lymphocytes has been shown to suppress immunoglobulin synthesis; in addition, generation of natural killer cell activity appears to be impaired. Moreover, there is evidence that the capability of polymorphonuclear leukocytes to generate oxygen radicals is diminished, perhaps directly by the virus or by activated regulatory T cells. This may further explain the enhanced susceptibility to bacterial superinfections. Virion components can be detected in biopsy specimens of Koplik's spots and vascular endothelial cells in the areas of skin rash. ^[33]
- In addition to necrosis and inflammatory changes in the respiratory tract epithelium, several other features of measles virus infection are noteworthy. The skin lesions show vasculitis characterized by vascular dilation, edema, and perivascular mononuclear cell infiltrates. The lymphoid tissues show hyperplastic changes, and large multinucleated reticuloendothelial giant cells are often observed (Warthin-Finkeldey cells). Some of the giant cells contain intracytoplasmic and intranuclear inclusions.

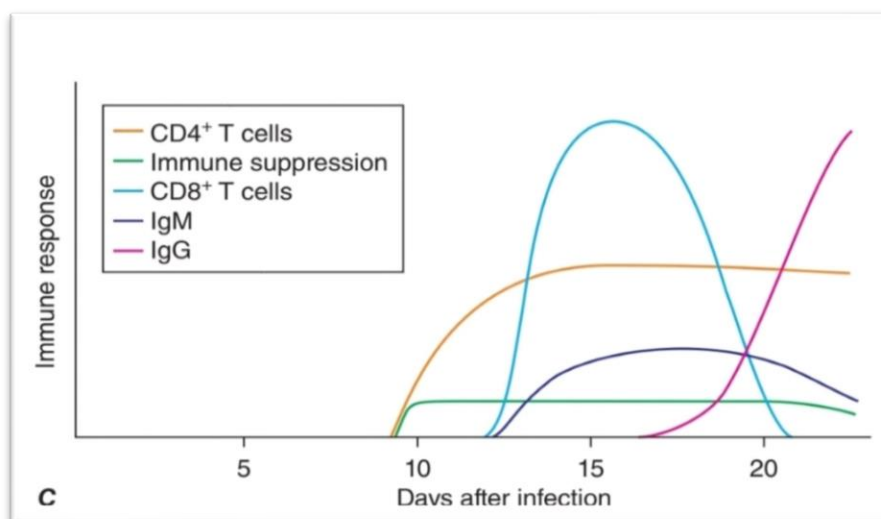


Figure (4): *Antibody and T cell responses to measles virus.*

The signs and symptoms of measles arise coincident with the host immune response.

- Similarly involved giant epithelial cells can be found in a variety of mucosal sites, the respiratory tract, skin, and urinary sediment.^[33]
- In some patients with measles, an immune-mediated post-infectious encephalitis occurs after the rash. The major findings in measles encephalitis include areas of edema, scattered petechial hemorrhages, perivascular mononuclear cell infiltrates, and necrosis of neurons.
- In most cases, perivenous demyelination in the CNS is also observed.^[33]
- **Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens^[34]:**
 - Measles virus infects immune cells, causing acute immune suppression, Measles caused elimination of 11 to 73% of the antibody repertoire across individuals. Recovery of antibodies was detected after natural re-exposure to pathogens. Notably, these immune system effects were not observed in infants vaccinated against MMR (measles, mumps, and rubella), but were confirmed in measles-infected macaques. The reduction in humoral immune memory after measles infection generates potential vulnerability to future infections, underscoring the need for widespread vaccination.
 - Immunosuppression was first documented when children with measles showed negative cutaneous tuberculin reactions after previously testing positive. Subsequent studies have shown decreased interferon signaling, skewed cytokine responses, lymphopenia, and suppression of lymphocyte proliferation shortly after infection. The MV receptor CD150/SLAMF1 (signaling lymphocytic activation molecule family member 1) is highly expressed on memory T, B, and plasma cells, resulting in their infection and depletion without an effect on total immunoglobulin G (IgG) levels. Recovery of the functional immune response, including resolution of lymphopenia, occurs 2 to 4 weeks after viral clearance. However, MV replication in immune cells has been hypothesized to impair immune memory, potentially causing “immunological amnesia”.
 - Epidemiological evidence has associated MV infections with increases in morbidity and mortality for as long as 5 years and suggests that in the pre-vaccine era, MV may have been associated with up to 50% of all childhood deaths from infectious diseases, mostly from non-MV infections. This phenomenon might be explained by immune amnesia. However, to date, no study has successfully resolved whether measles-induced immune amnesia a reduction in the diversity of the immune memory repertoire after measles infections indeed exists. To address this issue, we have studied paired blood samples collected before and

after MV infection using a sero-profiling tool that allows the detection of thousands of pathogen-specific antibodies.^[34]

- Measles virus(MV) should be considered as a predominantly lymphotropic and myelotropic virus. MV may use DCs as a vehicle to gain access to its main target cells in lymphoid tissues. Massive replication in CD150+ T- and B-lymphocytes then results in dissemination of the virus throughout the body. Preferential infection of memory lymphocytes leads to depletion of immunologic memory resulting in measles-associated immunosuppression.
- In addition, systemic infection of DCs may result in an impairment of antigen presentation functions. At the peak of virus replication high virus loads are present, which may spill over to other cell types that carry yet unidentified low affinity MV receptors. Further in vivo studies using recombinant morbilliviruses expressing fluorescent proteins will help elucidate the early events in MV infection, and can provide a scientific basis for vaccination strategies based on alternative routes of administration of the live-attenuated MV vaccine.^[35]
- **Pathogenesis:**

Measles virus is transmitted primarily by respiratory droplets over short distances and, less commonly, by small-particle aerosols that remain suspended in the air for long periods. Infection is initiated when measles virus is deposited in the respiratory tract, oropharynx, or conjunctivae.

During the first 2–4 days after infection, measles virus proliferates locally in the respiratory mucosa, primarily in dendritic cells and lymphocytes, and spreads to draining lymph nodes. Virus then enters the bloodstream in infected leukocytes, producing the primary viremia that disseminates infection throughout the reticuloendothelial system. Further replication results in secondary viremia that begins 5–7 days after infection and disseminates measles virus throughout the body. Replication of measles virus in the target

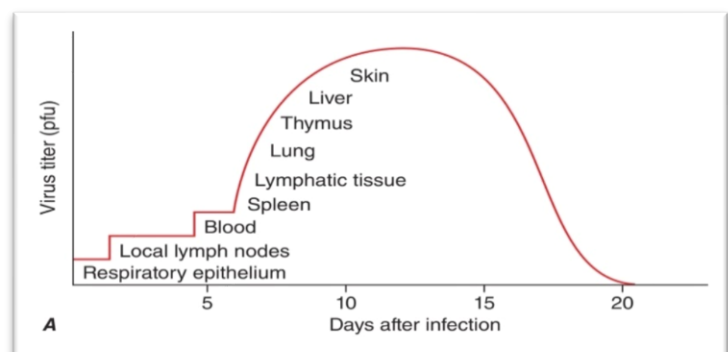


Figure (5): *Spread of measles virus, from initial infection of the respiratory tract through dissemination to the skin*

organs, together with the host's immune response, is responsible for the signs and symptoms of measles that occur 8–12 days after infection and mark the end of the incubation period. [27]

- **The incubation period**

The incubation period for measles is ~10 days to fever onset and 14 days to rash onset. This period may be shorter in infants and longer (up to 3 weeks) in adults. [29]

- **Differential Diagnoses** [29,37,38]

Healthcare provider may need to rule out other illnesses before diagnosing measles. Other illnesses they may rule out depend on how long patient been showing symptoms of measles.

Before the Rash Appears

During the few days before the measles rash appears, it may seem like patient have a respiratory virus such as the flu, respiratory syncytial virus (RSV), or a rhinovirus, which is typically the virus responsible for the common cold. Two to three days after symptoms begin, the Koplik's spots may appear in mouth, they can be mistaken for Fordyce spots, which are enlarged oil glands. However, fever is generally higher with measles than with other viral infections, which is one clue that patient don't have a typical viral infection. Measles can also be mistaken for dengue fever before or after the appearance of the rash, but this can be ruled out with a blood test.

After the Rash Appears

Once the rash has appeared three to five days after your other symptoms, other illnesses that healthcare provider may want to rule out could include: Roseola due to human herpes virus 6 or 7 result in a fever and rash, but the rash of Roseola (exanthem subitum) appear after fever has subsided. Rubella It's also called German measles or three-day measles. Rubella is caused by a different virus than measles, it is a milder illness without cough and with distinctive lymphadenopathy. Rubella rash fade rapidly. Parvovirus B19 infection presents with red “slapped” cheeks followed by a reticular rash on the trunk, arms, and legs. Adenovirus can cause fever and rash, along with conjunctivitis, pharyngitis, and coryza. Infectious mononucleosis: this viral infection may also present with similar symptoms, including a rash, particularly after taken certain antibiotics.

A blood test can rule out or confirm it. Other viruses include chickenpox and hand-foot-and-mouth disease. Usually, healthcare providers can easily rule these other viruses out by how rash looks, as well as other symptoms.

Scarlet fever and toxic shock syndrome (TSS): These group a Streptococcus infection cause rash as well, but scarlet fevers cause a blanching, erythematous, papular “sandpapery” (scarlatiniform) rash over the trunk, toxic shock syndrome can also present with fever and there is often conjunctival involvement. The rash is often a subtle, diffuse, macular erythema resembling gas unburn in the setting of a group A Streptococcus infection or Staphylococcus aureus infection.

TSS usually accompanied by low blood pressure and kidney problems. Reaction to drugs: A rash that's caused by hypersensitivity to a certain drug can look like a measles rash, but healthcare provider can quickly rule this out if patient haven't been recently exposed to any drugs. Meningococemia: This bacterial infection, which is caused by the same type of bacteria that causes meningitis, may have very similar symptoms to measles, including a maculopapular rash and irritability. This rash may disappear quickly or the patient may develop a petechial rash. A blood test will determine if patient have this infection or measles. Rocky Mountain spotted fever a tick-borne illness that can cause fever, headache, and a rash in a patient with a history of a tick bite, it's diagnosed with a blood test or skin biopsy. Noninfectious causes to consider include Kawasaki disease (KD) and systemic juvenile idiopathic arthritis (JIA). KD is an acute vasculitis that has specific diagnostic criteria but would include fever of 5 days or more, rash, and conjunctival injection. Systemic JIA may present with fever, arthritis, rash, and lymphadenopathy.

1.4 WHO IS AT RISK?

Measles virus is one of the most highly contagious directly transmitted pathogens. Outbreaks can occur in populations in which > 10 % persons are susceptible. Chains of transmission are common among household contacts, school-age children, and health care workers. Newborns become susceptible to measles virus infection when passively acquired maternal antibody is lost; when not vaccinated, these infants account for the bulk of new susceptible individuals.^[29]

- **People at high risk for severe illness and complications:**
 - Infants and children aged < 5 years.
 - Adult aged >20 years.
 - Pregnant women.
 - People with compromised immune systems, such as from leukemia and HIV-infection.^[39]
- **Risk Factors:**

Undernutrition is an important risk factor for developing more-severe measles complications. Some studies have suggested that the intensity of exposure (for example, transmission within households, health workers) is another important determinant of mortality. In addition, the period in which a person infected with MV remains infectious may be prolonged in individuals who are immunocompromised by severe undernutrition or HIV infection. The nutritional status of children with measles is, in turn, worsened by decreased food intake (particularly in children with mouth ulcers), increased metabolic demands of infection and gastrointestinal loss of nutrients. Malnutrition and vitamin A deficiency may be exacerbated by measles and can lead to keratitis, corneal scarring and blindness in children with severe vitamin A deficiency. Geographical differences in measles morbidity and mortality reflect variability in nutritional factors and access to high-quality health care, although host genetic factors, such as genes regulating cytokine production, might explain some differences in response to MV infection and vaccination. Studies of immune responses to measles vaccine suggest that polymorphisms in human leukocyte antigen (HLA) genes are associated with different antibody responses.^[40]

Breast-feeding may also be associated with a modest reduced risk for clinical measles infection up to the age of ten years.^[41]

There is also an environmental factor that contribute to the spread of the virus as its spread is common in certain seasons of the year like dry season in tropical zones, Winter in temperate climates (due to crowding).

1.5 MOOD OF TRANSMISSION

Measles virus is transmitted primarily by respiratory droplets over short distances and, less commonly, by small-particle aerosols that remain suspended in the air for long periods. Airborne transmission appears to be important in certain settings, including schools, physicians' offices, hospitals, and enclosed public places. The virus can be transmitted by direct contact with infected secretions but does not survive for long on fomites. ^[29]

Transmission occurs directly from person to person mainly by droplet infection and droplet nuclei (spread by coughing and sneezing). The virus is transmitted from person to person either by close personal contact or direct contact with infected nasal or throat secretions. The virus remains active and contagious in the air or on infected surfaces for up to 2 hours.

It can be transmitted by an infected person from 4 days prior to the onset of the rash to 4 days after the rash erupts. Infection can be transmitted through conjunctiva as well.

Recipients of measles vaccine are not contagious to others. Measles outbreaks can result in epidemics that cause many deaths. These deaths, especially occurring, among young, malnourished children. ^[30]

1.6 CLINICAL PICTURE

In most people, the signs and symptoms of measles are highly characteristic. Fever and malaise beginning ~10 days after exposure are followed by cough, coryza, and conjunctivitis. These signs and symptoms increase in severity over 4 days (Fig. 6).

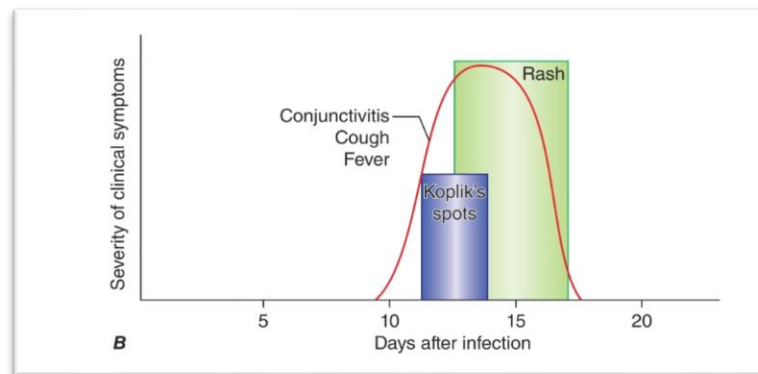


Figure (6): Severity of clinical symptoms

The virus causes systemic illness, sometimes including severe pneumonia, when primary infection occurs in an unvaccinated adult or an immunocompromised person of any age. Therefore, vigilance in maintaining high vaccination rates is critical. With primary infection, the illness in children is typically milder; however, mortality rates in lower-resource countries are high, especially among persons with underlying risk factors, including malnutrition.

Classic measles virus infection can be subdivided into the following clinical stages: **incubation, prodrome, exanthem, and recovery.**

1. Incubation period:

The incubation period for measles is 6 to 21 days (median 13 days) it begins after virus entry via the respiratory mucosa or conjunctivae. The virus replicates locally, spreads to regional lymphatic tissues, and is then thought to disseminate to other reticuloendothelial sites via the bloodstream, which is considered the first viremia. The period of contagiousness is estimated to be from five days before the appearance of rash to four days afterward. Infected individuals are characteristically asymptomatic during the incubation period, although some have been reported to experience transient respiratory symptoms, fever, or rash.

The dissemination of measles virus due to viremia, with associated infection of endothelial, epithelial, monocyte, and macrophage cells, may explain the variety of clinical manifestations and complications that can occur with measles virus infection. A second viremia occurs several days

after the first, coinciding with the appearance of symptoms signaling the beginning of the prodromal phase.

2. Prodromal period:

The prodromal period usually lasts for two to four days, it is defined by the appearance of symptoms that typically include fever, malaise, and anorexia, followed by conjunctivitis, coryza, and cough. The severity of conjunctivitis is variable and may also be accompanied by lacrimation or photophobia.

The respiratory symptoms result from mucosal inflammation from viral infection of epithelial cells. Fever is typically present. Various fever patterns have been described, and fever as high as 40°C can occur. The prodromal symptoms typically intensify a few days before the exanthema appears.

Enanthem: Approximately 48 hours prior to onset of the exanthem, patients may develop an enanthem characterized by Koplik's spots (1 to 2 mm white or bluish lesions with an erythematous halo on the buccal mucosa opposite the lower molars teeth, though they can spread to cover the buccal and labial mucosa as well as the hard and soft palate). They have been described as "grains of salt on a red background" are pathognomonic for measles (Fig.7).



Figure (7): *koplik's spots*

It is important to search carefully for Koplik's spots in patients with suspected measles, since they can improve the accuracy of clinical diagnosis. However, this enanthem does not appear in all patients with measles.

3. Exanthem period:

The exanthem of measles arises approximately two to four days after onset of fever; starts behind the ears, neck and the hairline and moves down the body to involve the face, upper trunk, lower trunk, and extremities, typically sparing the palms and soles. It begins as discrete erythematous maculopapular, blanching rash, which become confluent as the rash spreads (Fig.8).



Figure (8): *Exanthema of Measles*

Early on, the lesions are blanching; in the later stages, they are not. The rash may include petechiae; in severe cases, it may appear hemorrhagic. In children, the extent of the rash and degree of confluence generally correlate with the severity of the illness. The cranial to caudal progression of the rash is characteristic of measles but is not pathognomonic.

Other characteristic findings during the exanthematous phase include lymphadenopathy, high fever (peaking two to three days after appearance of rash), pronounced respiratory signs including pharyngitis, and non-purulent conjunctivitis. Uncommonly, patients with severe measles develop generalized lymphadenopathy and splenomegaly.

Clinical improvement typically ensues within 48 hours of the appearance of the rash. After three to four days, the rash fades slowly in the same order of progression as it appeared, usually beginning on the third or fourth day after onset. Resolution of the rash may be followed by desquamation, particularly in undernourished children.

Because the characteristic rash of measles is a consequence of the cellular immune response, it may not develop in persons with impaired cellular immunity (e.g., those with AIDS). These persons have a high case fatality rate and frequently develop giant-cell pneumonitis caused by measles virus. T lymphocyte defects due to causes other than HIV-1 infection (e.g., cancer chemotherapy) also are associated with increased severity of measles.

When the clinical manifestations are most severe, and signal the host's immune response to the replicating virus. Headache, abdominal pain, vomiting, diarrhea, and myalgia may be present.

4. Recovery and immunity:

Cough may persist for one to two weeks after measles. The occurrence of fever beyond the third to fourth day of rash suggests a measles-associated complication.

Both humoral and cellular measles-specific immunity are important for viral clearance and lasting protective immunity. Children with defects in humoral immunity, such as agammaglobulinemia, generally recover from measles, while individuals with T cell deficiencies often have severe measles infection and high mortality rates.

Immunity after measles virus infection is thought to be lifelong, although there are rare reports of measles reinfection.

- **Clinical variants**

- **Modified measles:**

Modified measles is an attenuated infection that occurs in individuals with pre-existing measles immunity (either via wild-type disease or vaccination). It is similar to classic measles except the clinical manifestations are generally milder and the incubation period is longer (17 to 21 days). Individuals with modified measles are not highly contagious.

- **Atypical measles:**

Individuals with atypical measles develop high fever and headache 7 to 14 days after exposure to measles. Atypical measles is characterized by higher and more prolonged fever. A maculopapular rash develops two to three days later, beginning on the extremities (instead of the head as seen with typical measles) and spreading to the trunk. The rash may involve the palms and soles and tends to spare the upper chest, neck, and head. The rash may be vesicular, petechial, purpuric, or urticarial; it may have a hemorrhagic component. The distribution and varied appearance of the rash can make diagnosis difficult.

A dry cough and pleuritic chest pain are often present; pneumonitis can be severe. Chest radiograph typically demonstrates bilateral pulmonary nodules and hilar lymphadenopathy. Atypical measles often results in severe illness; many individuals develop respiratory distress. Some individuals develop peripheral edema, hepatosplenomegaly, and/or neurologic symptoms such as paresthesia or hyperesthesia.

The pathogenesis of atypical measles is not entirely understood. A severe atypical measles syndrome was observed in recipients of a formalin- inactivated measles vaccine who were subsequently exposed to wild type- measles virus. Individuals with atypical measles do not appear to transmit measles virus to others. ^[29,42]

1.7 DIAGNOSIS

Measles is readily diagnosed on clinical grounds by clinicians familiar with the disease, particularly during outbreaks. Koplik's spots are especially helpful because they appear early and are pathognomonic.

Clinical diagnosis is more difficult:

- During the prodromal illness
- When the rash is attenuated by passively acquired antibodies or prior immunization
- When the rash is absent or delayed in immunocompromised children or severely undernourished children with impaired cellular immunity
- In regions where the incidence of measles is low and other pathogens are responsible for the majority of illnesses with fever and rash.

The CDC case definition for measles requires:

- A generalized maculopapular rash of at least 3 days' duration
- Fever of at least 38.3°C (101°F)
- Cough, coryza, or conjunctivitis.

Serology is the most common method of laboratory diagnosis. The detection of measles virus specific IgM in a single specimen of serum or oral fluid is considered diagnostic of acute infection, as is a fourfold or greater increase in measles virus-specific IgG antibody levels between acute- and convalescent-phase serum specimens. Primary infection in the immunocompetent host results in antibodies that are detectable within 1–3 days of rash onset and reach peak levels in 2–4 weeks. Measles virus-specific IgM antibodies may not be detectable until 4–5 days or more after rash onset and usually fall to undetectable levels within 4–8 weeks of rash onset. false-positive results were found to result from human parvovirus B19 IgM.

Anti-measles IgG is generally undetectable up to 7 days after rash onset but subsequently peaks about 14 days after the exanthema appears. Several methods for measurement of antibodies to measles virus are available. Neutralization tests are sensitive and specific, and the results are highly correlated with protective immunity; however, these tests require propagation of measles virus in cell culture and thus are expensive and laborious. Commercially available enzyme immunoassays are most frequently used. Measles can also be diagnosed by isolation of the virus

in cell culture from respiratory secretions, nasopharyngeal or conjunctival swabs, blood, or urine during the prodromal phase. However, culture of the virus requires special facilities. Viral isolates are important for molecular epidemiologic surveillance. Direct detection of giant cells in respiratory secretions, urine, or tissue obtained by biopsy provides another method of diagnosis.

For detection of measles virus RNA by reverse-transcription polymerase chain reaction amplification of RNA extracted from clinical specimens, primers targeted to highly conserved regions of measles virus genes are used. Viral RNA is usually present for approximately three days after rash onset. Extremely sensitive and specific, this assay may also permit identification and characterization of measles virus genotypes for molecular epidemiologic studies and can distinguish wild-type from vaccine virus strains. ^[29,42]

1.8 COMPLICATIONS

The complications of measles can be many and varied, and more serious than people might realize.

Measles can be serious in all age groups. However, there are several groups that are more likely to suffer from measles complications:

- Children younger than 5 years of age.
- Malnutrition and poverty.
- Vitamin A deficiency.
- Adults older than 20 years of age.
- Pregnant women.

People with compromised immune systems, such as from leukemia or HIV infection.^[43]

Common complications:

1- Pneumonia:

The depression of cellular immunity that follows measles, especially in children with subnormal vitamin A reserves, often allows a supervening bacterial or viral infection of the respiratory tract. The usual culprits are Adenovirus, Herpes simplex or Staphylococcus aureus. Supervening Adenovirus and Herpes Simplex virus infections are known to have a severe necrotizing effect on tissues and infection is persistently relapsing.

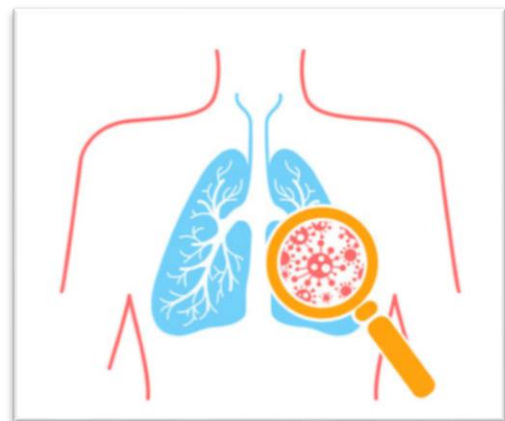


Figure (9): *Pulmonary Complications*

The muscle and elastic of bronchioles and bronchi are especially vulnerable to destruction. Prolonged ongoing destruction of bronchioles usually leads to antibiotic-resistant bacterial infection with the development of lung abscesses, peri-bronchial fibrosis and ultimately cor-pulmonale.^[44]

Persistent infection with a giant cell pneumonitis, due to replication of measles virus in the lungs can develop in immunocompromised children, including those with HIV1 infection.

2- Central Nervous System complications:

Neurologic complications are relatively infrequent, but important, causes of disability and death due to measles. These complications have different pathogenic mechanisms and host susceptibilities.

Apparently uncomplicated measles is frequently accompanied by a cerebrospinal fluid (CSF) pleocytosis and electroencephalogram changes suggesting the possibility of relatively frequent subclinical involvement of the CNS during infection.^[44]

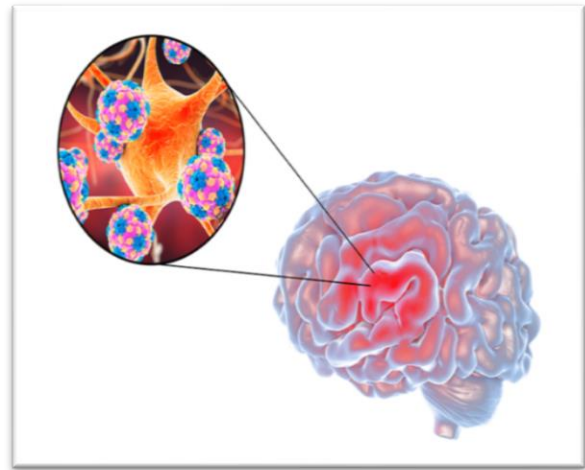


Figure (10): *Measles virus attacks brain cells*

Encephalitis is irritation and swelling (inflammation) of the brain. Post-measles encephalomyelitis complicates ~1 in 1000 cases, affecting mainly older children and adults. Encephalomyelitis occurs within 2 weeks of rash onset and is characterized by fever, seizures, and a variety of neurologic abnormalities.

The finding of periventricular demyelination, the induction of immune responses to myelin basic protein, and the absence of measles virus in the brain suggest that post-measles encephalomyelitis is an autoimmune disorder triggered by measles virus infection. Encephalitis may occur right after measles, or it might not occur until months later. Encephalitis can cause permanent brain damage. About 15 percent of people who develop measles encephalitis will die. Up to one-quarter will have ongoing brain damage afterward. The most common cause of measles-related death children is pneumonia. In adults, it's encephalitis.

It has been hypothesized that various mutations of measles virus may help in neuro invasion without any need of receptors. These mutated virus particles have been isolated from either autopsy or biopsy of brain tissue of patients of complicated measles infection. (see table 3)

Table (3): Mutations of measles virus reported to cause neuro invasion ^[46]

Protein	Mutation	Effect	Disease
M protein	Biased hypermutation of M protein (uridine to cysteine substitution)	More fusogenic phenotype without budding making it more suitable for CNS infection	SSPE, MIBE
	RNA mutation causing low expression of M protein		
F protein	HRC domain (T461I, A440P, N462S, N465S) HRN domain (G168R/ E170G), (S262G), cytoplasmic tail domain (R520C, L550P), F2 subunit of F protein. F extracellular domain (T461I, S103I/N462S/N465S)	Hyperfusogenic F protein which allows entry in brain without receptors	SSPE
	HRC domain L454W	Highly unstable and hyperfusogenic F protein, not requiring receptor for invasion	MIBE
H protein	Substitution mutations cytoplasmic tail (R7Q) stalk domain (R62Q), and five blade of the head domain (D530E) C-terminus elongation of the H protein due to single-point mutation at the stop codon	Contributes neurovirulence impact binding, targeting	SSPE
	Mutations in H gene of MIBE	Less frequently dementated	MIBE
	N, P and L proteins		SSPE, MIBE

3-types of CNS complications: (see table 4):

- ❖ Measles inclusion body encephalitis (MIBE): is a rare but fatal complication and typically occurs months after infection. It's due to progressive measles virus infection of the nervous system and occurs in immune-compromised individuals who are unable to clear virus after infection. Disease onset is subacute and usually fatal. Pathology shows nuclear and cytoplasmic viral inclusion bodies with little evidence of inflammation. ^[45]
- ❖ Long-term complications: subacute sclerosing panencephalitis (SSPE): is a slowly progressive, disabling, and deadly brain disorder disease characterized by seizures and progressive deterioration of cognitive and motor functions. (SSPE) is a very rare, but fatal disease of the central nervous system that results from a measles virus infection acquired earlier in life. SSPE generally develops 7 to 10 years after a person has measles, even though the person seems to have fully recovered from the illness. The risk of developing SSPE may be higher for a person who gets measles before they are 2 years of age. ^[45]

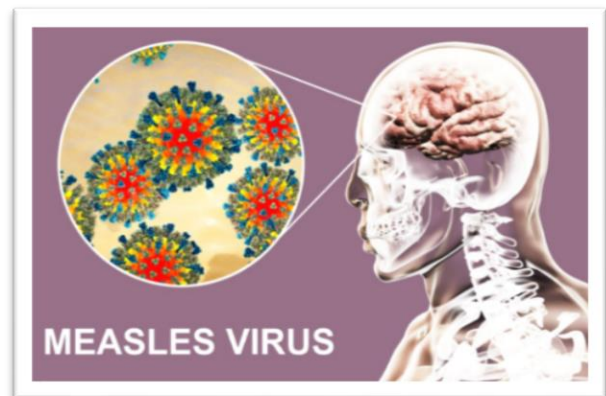


Figure (11): *Measles inclusion body Encephalitis*

SSPE has been reported in all parts of the world, but in western countries it is a rare disease. Males are more often affected than females. The disease generally occurs in children and adolescents.

Symptoms of SSPE occur in four general stages. With each stage, the symptoms are worse than the stage before:

Stage I: There may be personality changes, mood swings, or depression. Fever and headache may also be present. This stage may last up to 6 months.

Stage II: There may be uncontrolled movement problems including jerking and muscle spasms. Other symptoms that may occur in this stage are loss of vision, dementia, and seizures.

Stage III: Jerking movements are replaced by twisting movements and rigidity. Death may occur from complications.

Stage IV: Areas of the brain that control breathing, heart rate, and blood pressure are damaged. This leads to coma and then death.

- Primary measles encephalitis (PME): The measles virus directly infects CNS during acute measles infection in a previously healthy child, leading to measles encephalitis. The virus replicates in brain cells and leads to injury of neurons, which further causes lymphocytic infiltration in brain parenchyma, meninges, and CSF, hence, the infectious measles virus can be detected from brain cells and CSF.
- Acute post measles encephalitis (APME): It is also referred to as acute measles encephalitis (AME), acute demyelinating encephalomyelitis (ADEM), or post infectious encephalitis (PIE) or acute disseminated encephalomyelitis. The encephalitis is immune mediated unlike PME which is due to direct viral invasion. The molecular mimicry has been suggested as the mechanism for the development of APME. Circulating antibodies react with the myelin basic protein of oligodendrocytes, causing inflammation and dysfunction in CNS. APME causes lesions in both grey and white matter, leading to perivenular inflammation and demyelination (see table 4).

The clinical profile and characteristics of measles virus in each disease are discussed below and summarized in (table 5).

Immunoglobulin titers in CSF as compared to that in the serum do not increase, suggesting less synthesis of antibodies in CSF. Myelin basic protein concentrations are increased in CSF and nearly (50%) of the patients show lymphocyte proliferative responses to myelin basic protein. It is primarily an immune-mediated demyelinating disease, however, the role of myelin reactive antibodies is still unclear, there are many unanswered questions regarding the neurologic complications of measles, recent advances have led to better understanding of the mechanism of the spread of measles within the nervous system, particularly the disruption of F protein function, which raises the possibility of treatment with fusion-inhibiting molecules.^[44]

Table (4): Incidence of measles related CNS complications after natural measles infection and after vaccination. ^[46]

Disease	Incidence after measles infection	Incidence after vaccination	Morbidity and mortality
PME	1-3/1,000	<1 per 100,000 less fulminant	Mortality: 10 to 15%, permanent neurological sequelae in 25%, with epilepsy and intellectual disability
APME	1/1,000	1-2/100,000 less fulminant	Some have a full recovery, while few are left with substantial neurological sequelae
MIBE	Rare (only in Immunocompromised patient)	<1 per 100,000	Mortality: 75% Rest have poor neurological outcomes
SSPE	4-11/100,000	0	Mortality: 100%

Table (5): the clinical profile and characteristics of measles virus in each disease.

	PME	APME	MIBE	SSPE
Measles infection (active/passive)	Active measles infection	Post infectious	Active measles infection in patients who are immunosuppressed	Measles infection early childhood, no active infection now.
Temporal relation of onset with measles infection	During acute exanthem phase	During resolution phase or weeks/ months after measles infection or vaccination?	Onset within a year of infection or measles vaccination?	Occurs after 3-20 years of infection _although shorter latency periods reported recently
Mechanism of disease	Measles virus enters the brain causing lymphocytic infiltration	Molecular mimicry mediated immune response	Persistence of primary measles infection	Persistence of mutated measles virus
Age group	More common in children than in adults	Most common in children and adolescents, rare in adults	Any age, More common in children and young adults	Usually 8-11 years, can be seen in toddlers and adults
Clinical features	fever, headache, irritability encephalopathy, seizures, involuntary movements or	Encephalitis (seizures, altered sensorium, raised ICT), myelitis (back pain and bladder and bowel dysfunction, hyporeflexia),	No rash, encephalopathy, refractory seizures, motor deficits	Behavioral problems, motor dysfunction, spasticity, myoclonic jerks, ocular involvement

	motor deficits and coma	ataxia, optic neuritis		
EEG	Focal or generalized Epileptiform discharges or diffuse slowing	Either normal or non-specific changes	Focal or generalized epileptiform discharges or diffuse slowing	Burst suppression, diffuse slowing
Neuroimaging	Focal signal changes on T2 images and edema	Multifocal hyperintensities in brain and spinal cord, brain edema, demyelination	Initially normal, later edema, atrophy or ventriculomegaly can be seen	hyperintensities in cerebral cortex, periventricular white matter, brainstem, cortical atrophy and ventriculomegaly
Neuropathology	Lymphocytic infiltration, inflammation, raised Intracranial tension	Perivenular demyelination and inflammation	Inclusion bodies in neurons and glial cells, focal necrosis without inflammation	Cellular inclusion bodies, demyelination, neuronal loss
CSF picture	Marked lymphocytosis with elevated proteins, normal glucose levels	Mild to moderate lymphocytosis with elevated proteins, normal glucose levels	Usually normal, later can show mild pleocytosis or raised proteins	normal

Isolation of measles virus from brain cells	Can be isolated from brain cells and CSF	Cannot be isolated	Can be isolated	Mutated virus can Be isolated
Serology	Measles specific antibodies may or may not be detected in serum and CSF	Myelin basic protein (MBP) is raised in CSF	Rising titers of measles specific antibodies in serum and CSF	Markedly raised measles antibodies in serum and CSF
Treatment	Symptomatic treatment, anticonvulsants, ribavirin	Symptomatic treatment and Immunosuppression with steroids, plasmapheresis and IVIG	Symptomatic, ribavirin, interferon alpha	Symptomatic, ribavirin, interferon alpha

4-Ear infections: (otitis media) occur in about one out of every 10 children with measles. One of the most common complications of measles is a bacterial ear infection. ^[47]



Figure (12): *Ear complication*

5-Diarrhea: is reported in less than one out of 10 people with measles. Diarrhea and vomiting can result in losing too much water from the body (dehydration). ^[47]

6-Complications of measles during pregnancy:

The incidence of death and other complications from measles during pregnancy may be higher than expected for age-comparable, non-pregnant women. Measles in pregnancy may lead to high rates of fetal loss and prematurity, especially in the first 2 weeks after the onset of rash. ^[49]

The most common and serious maternal complication was pneumonitis. Other maternal complications included hepatitis, premature labor, spontaneous abortion, and death. Historical accounts describing maternal sequelae of measles have suggested more severe disease in pregnant women, although this observation has not always been confirmed by more recent reports in developed countries. The clinical course in our patients suggests that measles during pregnancy may be associated with serious complications.

7-Membranous laryngotracheobronchitis: is a very serious infection which affects the larynx, trachea and bronchi, requiring aggressive therapeutic measures. It has been recently rediscovered as a cause of disease in children. However, it is a very unusual complication of measles. Two infants with measles and membranous laryngotracheobronchitis are reported. ^[48]

Also, complications of measles can include hepatitis, appendicitis, and viral meningitis. In 2017 the global death toll from measles reached 110,000. Most of these deaths were in young children.

1.9 TREATMENT

The treatment of Measles virus is not feasible due to the inability of the drugs to eradicate the virus. Therefore, the treatment is solely based on managing the symptoms of the disease. Treatment depends on the patient's symptoms, age, and general health. It will also depend on how severe the condition is. Caregiving worker should focus on relieving symptoms, making the patient comfortable and preventing complications.

Providing adequate water and treatments for dehydration can restore fluids lost due to diarrhea or vomiting. Eating a healthy diet to restore the vitamins, minerals is also important. ^[50]

For other symptoms that can be seriously dangerous on the child health, these instructions could be used for improvement of these symptoms.

Paracetamol or ibuprofen can help manage a fever, aches, and pains.

Encourage the child to rest and staying in bed. this is also important in preventing prevalence of the virus to others

A cool-mist vaporizer is helpful in reducing cough. Use a humidifier or put a wet towel on a warm radiator to moisten the air. A warm lemon and honey drink may help, but do not give honey to babies under 1 year.

For eyes symptoms, remove any crustiness with cotton wool soaked in water. Dim the lights if the eyes are hypersensitive. ^[54-55]

Antibiotic medicine for bacterial infections that may develop. Antibiotics don't treat viral infections like measles. But they can treat a complication such as a bacterial infection. ^[55]

Because secondary bacterial infections are a major cause of morbidity and death attributable to measles, effective case management involves prompt antibiotic treatment for patients who have clinical evidence of bacterial infections, including pneumonia and otitis media. Streptococcus pneumonia and Hemophilus influenzae (type b) are common causes of bacterial pneumonia following measles, vaccines against these pathogens probably lower the incidence of secondary bacterial infections following measles. ^[51]

Intravenous ribavirin has been suggested for patients with severe measles pneumonia and of immunocompromised patients with measles encephalitis However, the clinical benefits of ribavirin in measles have not been conclusively demonstrated in clinical trials. ^[56]

Patient must be isolated for 4 days from the onset of rash, if the patient is immunocompromised the isolation must be longer. ^[56]

Measles is a viral disease that infects and damages these tissues. Vitamin A deficiency is known to depress the immune function and destroy epithelial tissue, and measles produces similar effects. The combined effect of vitamin A deficiency and measles infection could be serious. Therefore, when a child who has marginal vitamin A stores contracts measles, the already depleted vitamin A stores are exhausted, thereby reducing the ability to resist secondary infections or their consequences. This would also further accentuate the reduction of immunocompetence that is associated with measles infection.

Vitamin A is effective for the treatment of measles and can markedly reduce rates of morbidity and mortality, also it can help prevent eye damage and blindness. All children or adults with measles should receive enough supplement of vitamin A. This restores low vitamin A-levels that occur even in well-nourished children. ^[50]

The WHO recommends administration of once-daily doses of 200,000 IU of vitamin A for 2 consecutive days to all children with measles who are ≥ 12 months of age. Lower doses are recommended for younger children: 100,000 IU per day for children 6–12 months of age and 50,000 IU per day for children < 6 months old (see table 6). ^[51]

Vitamin A treatment in developing countries has decreased mortality and morbidity in these countries. A child who doesn't have enough vitamin A may need to take extra doses of this vitamin. Vitamin A does not treat measles by itself, but it prevents the bad outcomes tied to vitamin A deficiency. It lessens the chance of serious complications and death. Since most people don't know if they are lacking in vitamin A, a child's healthcare provider will probably give child extra vitamin A if he or she has measles. ^[52]

Table (6): *WHO recommendation of vitamin A doses in particular age group* ^[51]

Age group	Dose (IU)	Frequency
< 6	50,000 IU	One daily dose for two consecutive days
6-12	100,000 IU	
≥ 12	200,000 IU	

A third dose is recommended 2–4 weeks later for children with evidence of vitamin A deficiency.

While such deficiency is not a widely recognized problem in the United States, many American children with measles do, in fact, have low serum levels of vitamin A, and these children experience increased measles-associated morbidity. The Committee on Infectious Diseases of the American Academy of Pediatrics recommends that the administration of two consecutive daily doses of vitamin A be considered for children who are hospitalized with measles and its complications as well as for children with measles who are immunodeficient; who have ophthalmologic evidence of vitamin A deficiency, impaired intestinal absorption, or moderate to severe malnutrition; or who have recently emigrated from areas with high measles mortality rates. Parenteral and oral formulations of vitamin A are available.^[50]

There are studies show the efficacy of vitamin A in treatment of measles. Vitamin A did not have a clear effect on overall mortality rates. However, it reduced the risk of death from measles by 87% for children younger than two years old. In addition, for all children, it reduced the length of time the child suffers from diarrhea by 2 days and shortens the duration of fever by 1 day.

Vitamin A deficiency is more common in low-and middle-income countries putting children with measles in these countries at greater risk of severe infection. Providing children with measles in these countries with vitamin A can prevent measles-related deaths and complications.^[53]

1.10 LAST STATISTICS OF MEASLES IN YEMEN

Measles is a highly contagious disease spreading dramatically fast among people leading to many outbreaks throughout the world. In Yemen, recent conflict and war led to collapse of the health system that leads to decrease of immunization coverage, and most important of all the poor health education among people and the false ideas towards the vaccines which leads to increase the reported measles cases in the last few years.

In this year (2023), from January to the first week of September, regarding to the data collected from General Administration for Disease Control and Epidemiological Surveillance-National surveillance program for Measles and Rubella in Yemen, the number of suspected Measles and Rubella cases reached 22019 case including 241 deaths, compared to 22287 cases and 167 associated deaths in the whole year of 2022(see figure13), and 9947 case including 73 deaths in the hole year of 2021.

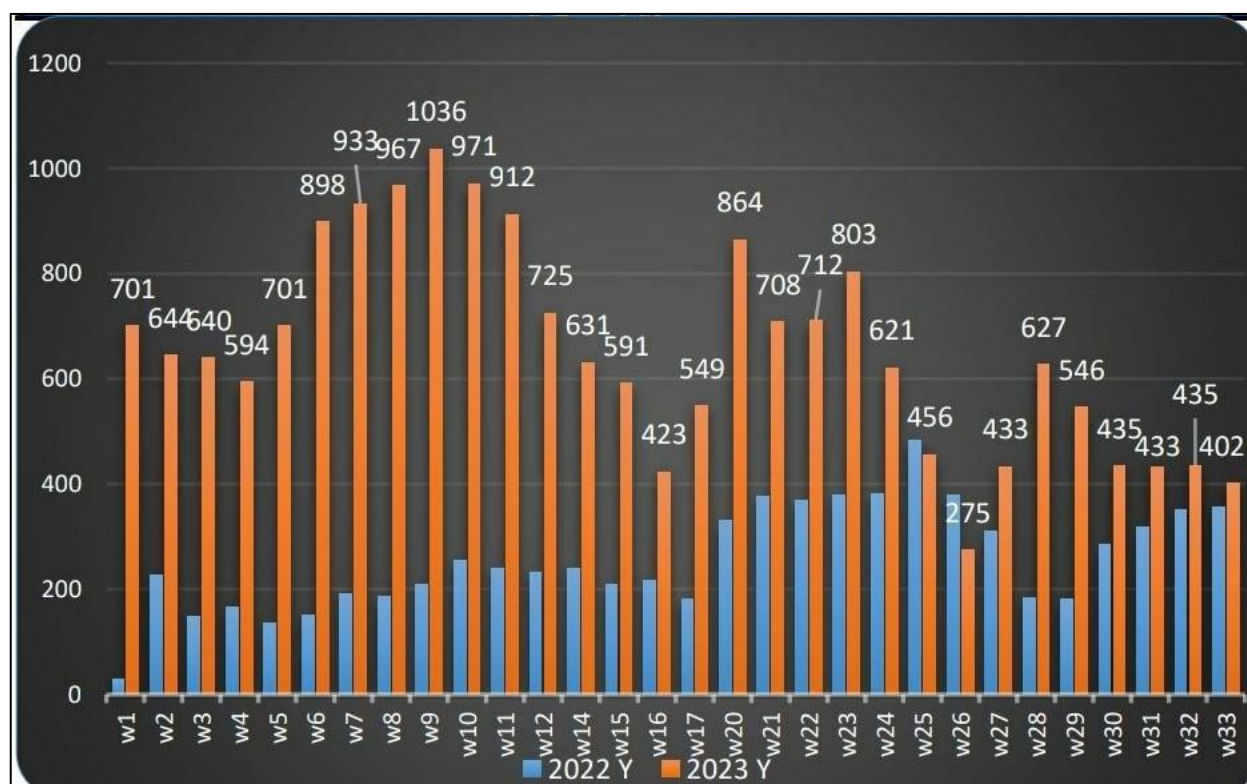


Figure (13): Suspected measles and rubella cases in 2022 and 2023

Huge increase that we witnessed this year cannot be ignored as the number of cases has almost tripled compared to the last two years. As mentioned before the major gaps in routine vaccination campaigns and economic difficulties, fueled by violent conflict, in addition to limited access to basic health care facilities and the increase pressure on the accessible healthcare facilities play a major role in the spread of measles and other preventable diseases.

From the beginning of the 2023 to the 33th week of the year, suspected measles and rubella cases are 22019. laboratory samples were collected from 6051 (27% of the total number of the reported cases), 1118 (63%) of the laboratory tested cases were confirmed, and 633 (3%) were discarded. (see figure 14)

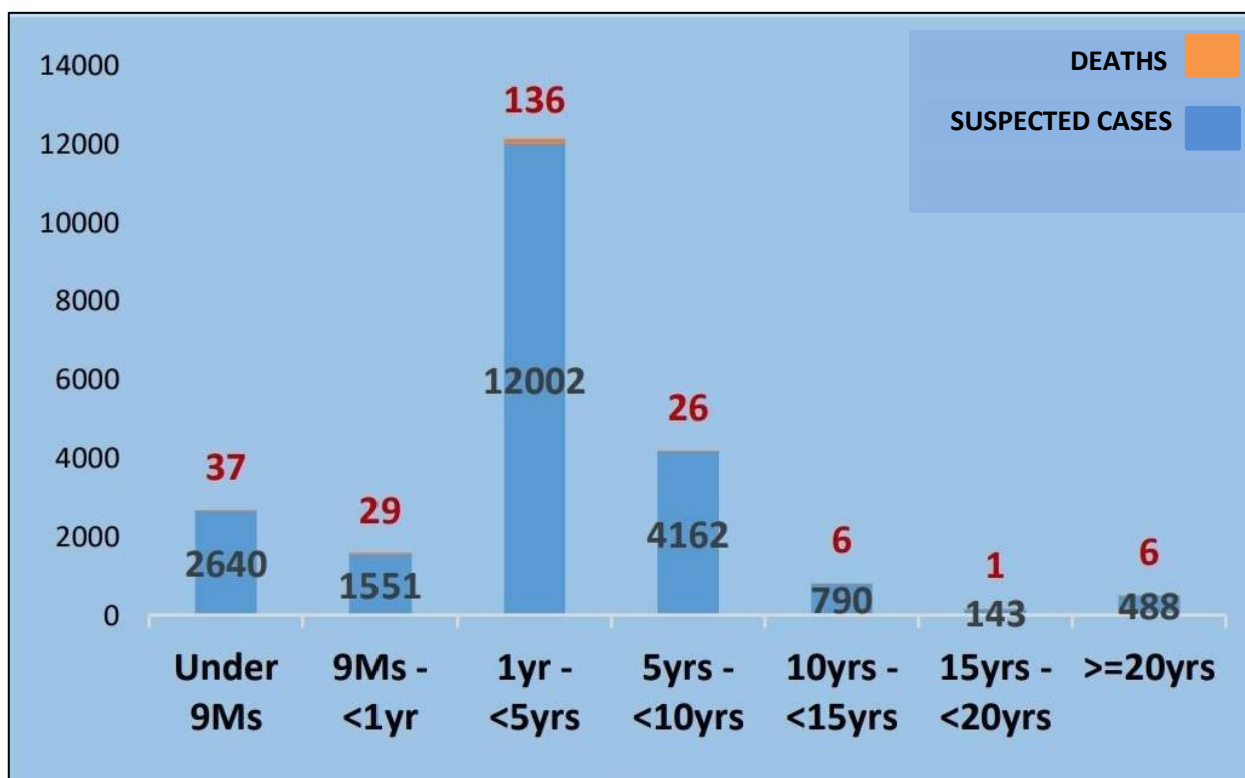


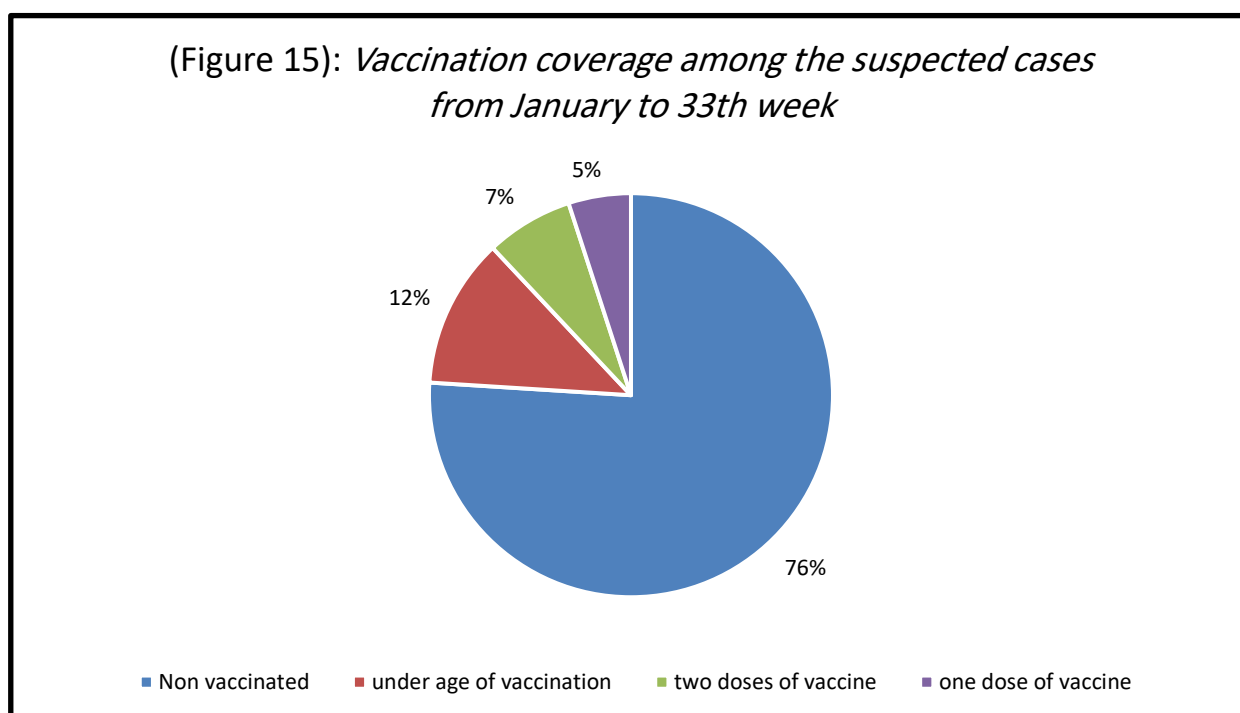
Figure (14): Suspected cases and deaths among the different age groups until the 33th week of year 2023

Sa'adah governorate takes the highest number of these suspected cases (3798case) followed by Al-Bayda and Hajjah governorates. However, Amanat Al-Asimah takes the highest number of laboratory confirmed cases(290case) which may be due to the available medical facilities.

The number of deaths due to measles complications from the beginning of the year(2023) until the end of the week (33) reached 241 deaths: 21 Sanaa, 23 Dhamar, 14 Sa'ada, 15 Amanat Al-Asimah, 18 Al-Bayda, 2Raymah, 41 Hajjah, 46 Al-Hodeidah, 10 Ibb, 6 Al-Dhalea, 2 Marib, 11 Al-Jawf, 16 Imran, 3 Al-Mahwit and 13 Taiz, which is increasing compared to deaths in 2022 that were 167 in the whole year, (162 to the 52th weeks: 16 Sana'a, 19 Thamar, 11 Al-Jawf, 14 Aden, 11 Sa'adah,1 Al-Mokala, 8 Amana Al-Asimah, 30 Al-Bayda, 1 Abyan, 1 Lahj, 1 Taiz, 7 Hajjah, 1 Marib, 12

Al-Hodeidah, 11 Ibb, 5 Amran, 10 Al-Dhalea, 1 Socatra and 5 death were reported in the 53th week of 2022. Children under five years has the highest mortality rate in both years.)

The finding shows that females were more affected than males in nearly all age groups. Furthermore, the data shows that under five years old children were the most affected age group (611 cases) among the laboratory confirmed cases (1118 cases). The collected data also shows that (76%) of the measles and rubella suspected cases were unvaccinated, (12%) under the age of vaccination, (5%) had only the first dose of the vaccine, and only (7%) had two doses or more of the vaccines. (see figure 15)



SECTION 2

Prevention and Statistics of Measles Virus Vaccination in Yemen

2.1 PREVENTION

Background:

Measles has been preventable through vaccination since a vaccine was licensed in 1963. People who do not have evidence of measles immunity should be considered at risk for measles, particularly during international travel. Acceptable presumptive evidence of immunity to measles includes birth before 1957; laboratory confirmation of disease; laboratory evidence of immunity; or written documentation of age-appropriate vaccination with a licensed, live attenuated measles-containing vaccine, namely, MMR or measles-mumps-rubella-varicella (MMRV). For infants 6 months old and older, but younger than 12 months, this includes documented administration of one dose of MMR; for people aged ≥ 12 months, documentation should include 2 doses of MMR or MMRV (the first dose administered at age ≥ 12 months and the second dose administered no earlier than 28 days after the first dose). Verbal or self-reported history of vaccination is not considered valid presumptive evidence of immunity.^[57]

From 1963–1967, a formalin-inactivated measles vaccine was available in the United States and was administered to $\approx 600,000$ – $900,000$ people. It was discontinued when it became apparent that the immunity it produced was short-lived. Consider people who received this vaccine unvaccinated.^[57]

Public education

To encourage measles immunization

Improvement of the nutrition status.

Active measles immunization:

Vaccination

Measles vaccine contains live, attenuated measles virus, which in the United States is available only in combination formulations (e.g., MMR and MMRV vaccines). MMRV vaccine is licensed for children aged 12 months – 12 years and can be used in place of MMR vaccine if vaccination for measles, mumps, rubella, and varicella is needed.^[57]



Figure (16): Measles vaccine

International travelers, including people traveling to high-income countries, who do not have presumptive evidence of measles immunity and who have no contraindications to MMR or MMRV, should receive MMR or MMRV before travel.^[57]

In 1963, both an inactivated (“killed”) and a live, attenuated (Edmonston B strain) measles vaccine were licensed for use in the United States. The inactivated vaccine was withdrawn in 1967 because it did not protect well against measles. The original Edmonston B vaccine was withdrawn in 1975 because of a relatively high frequency of fever and rash in recipients. A live, further attenuated (Schwarz strain) vaccine was first introduced in 1965, but also is no longer used in the United States. Another live, further attenuated strain (Edmonston-Enders strain) vaccine was licensed in 1968. These further attenuated vaccines caused fewer reactions than the original Edmonston B vaccine. In 1971, measles vaccine was licensed as a combined measles, mumps, and rubella (MMR) vaccine. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed.^[57]

Characteristics of vaccine

MMR vaccine is a lyophilized preparation of measles virus vaccine live, an attenuated line of measles virus, derived from Enders’ attenuated Edmonston strain and propagated in chick embryo cell culture; mumps virus vaccine live, the Jeryl Lynn strain of mumps virus propagated in chick embryo cell culture; and rubella virus vaccine live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts. MMRV vaccine contains measles, mumps, and rubella virus of equal titer and identical to those in the MMR vaccine. The titer of Oka varicella zoster virus is higher in MMRV vaccine than in single-antigen varicella vaccine, a minimum of 9,772 plaque-forming units (PFU) versus 1,350 PFU, respectively.^[57]

MMR and MMRV vaccines are supplied as a lyophilized (freeze-dried) powder and are reconstituted with sterile, preservative-free water. Both vaccines contain gelatin. MMR and MMRV vaccines are administered by the subcutaneous route. Each dose of MMR and MMRV vaccine contains neomycin as an antibiotic. It contains no adjuvant or preservative.^[57]

Figure (17): Measles vaccine characteristics ^[57]:

- ✓ Live, attenuated vaccine
- ✓ Available as lyophilized powder
- ✓ and reconstituted with sterile, preservative-free water
- ✓ Administered by subcutaneous injection

Vaccination Schedule and Use:

Infants (6 months old and older, but younger than 12 months):

One MMR dose. Infants vaccinated before age 12 months must be revaccinated on or after the first birthday with 2 doses of MMR or MMRV separated by ≥ 28 days. MMRV is not licensed for children aged <12 months.^[57]

Children (aged ≥ 12 months):

2 doses of MMR or MMRV separated by ≥ 28 days.

Adults born in or after 1957:

2 doses of MMR separated by ≥ 28 days.

One dose of MMR is $\approx 85\%$ effective when administered at age 9 months; MMR and MMRV are 93% effective when administered at age ≥ 1 year.

The vaccination in Yemen according the expanded immunization program.

In Yemen, the vaccination is administered in three doses. The first dose is given at 9 months of age, the second dose at 18 months, and a booster dose upon entering school.

- Name of vaccine: MR.
- Type and content: live, an attenuated virus.
- Dose: 0.5 ml.
- The vaccine vial: 10 dose.
- The storage temperature of the vaccine: $+2$ to $+8$ degrees.
- The vaccine is affected by freezing: not spoilage.
- The effectiveness of the vaccine after completing the doses: 95%.

Revaccination

Revaccination is recommended for certain persons. The following groups should be considered unvaccinated and should receive at least 1 dose of measles vaccine:

- 1) persons vaccinated before their first birthday.
- 2) persons vaccinated with killed measles vaccine.
- 3) persons vaccinated from 1963 through 1967 with an unknown type of vaccine.
- 4) persons who received immune globulin (IG) in addition to a further attenuated strain or vaccine of unknown type.
- 5) persons with perinatal human immunodeficiency virus (HIV) infection who were vaccinated before establishment of effective antiretroviral therapy (ART) and who do not have evidence of current severe immunosuppression.^[57]

Measles, mumps or rubella virus-containing vaccine administered prior to age 12 months (e.g., for international travel) should not be counted as part of the 2-dose series. Children vaccinated before age 12 months should be revaccinated with 2 doses of appropriately spaced MMR or MMRV vaccine, the first dose administered when the child is age 12 through 15 months (12 months if the child remains in an area where disease risk is high) and the second dose at least 4 weeks later. Persons who experienced perinatal HIV infection who may have received MMR vaccine prior to the establishment of effective combined antiretroviral therapy (cART) should be revaccinated with 2 appropriately spaced doses of MMR (i.e., the dose does not count) unless they have other acceptable current evidence of immunity. MMR series should be administered once effective cART has been established for at least 6 months and there is no evidence of severe immunosuppression.^[57]

Measles Immunity

Generally, persons can be considered immune to measles if they were born before 1957, have serologic evidence of measles immunity (equivocal test results should be considered negative), or laboratory confirmation of disease, or have documentation of adequate vaccination for measles⁵⁷.

Immunogenicity and Vaccine Efficacy

Measles antibodies develop in approximately 95% of children vaccinated at age 12 months. Seroconversion rates are similar for single-antigen measles, MMR vaccine, and MMRV vaccine.^[57]

Approximately 2% to 7% of children who receive only 1 dose of MMR vaccine fail to respond to it, i.e., they experience primary vaccine failure. MMR vaccine failure can occur because of passive antibody in the vaccine recipient, immaturity of the immune system, damaged vaccine, or other reasons. Most persons who fail to respond to the first dose will respond to a second dose. Studies indicate that more than 99% of persons who receive 2 doses of measles vaccine (with the first dose administered no earlier than the first birthday) develop serologic evidence of measles immunity. Although the titer of vaccine-induced antibodies is lower than that following natural disease, both serologic and epidemiologic evidence indicate that vaccine-induced immunity appears to be long-term and probably lifelong in most persons.^[57]

Most vaccinated persons who appear to lose antibody show an anamnestic immune response upon revaccination, indicating that they are probably still immune. Although revaccination can increase antibody titer in some persons, available data indicate that the increased titer may not be sustained. Some studies indicate that waning immunity may occur after successful vaccination, but this appears to occur rarely and to play only a minor role in measles transmission and outbreaks.^[57]

Adverse Reactions

In rare circumstances, MMR vaccination has been associated with anaphylaxis (≈ 2 –14 occurrences per million doses administered); febrile seizures (≈ 1 occurrence per 3,000–4,000 doses administered, but overall, the rate of febrile seizures after measles-containing vaccine is much lower than the rate with measles disease); thrombocytopenia (≈ 1 occurrence per 40,000 doses during the 6 weeks after immunization); or joint symptoms (arthralgia develops among $\approx 25\%$ of nonimmune postpubertal females from the rubella component of the MMR vaccination, and $\approx 10\%$ have acute arthritis-like signs and symptoms that generally persist for 1–21 days and rarely recur; chronic joint symptoms are rare, if they occur at all). No evidence supports a causal link between MMR vaccination and autism, type 1 diabetes mellitus, or inflammatory bowel disease.^[57]

Measles Vaccine Safety:

MMR

- Fever of 103°F (39.4°C) or higher 5%–15%
- Rash 5%
- Febrile seizures 1 in every 3,000 to 4,000 doses

- Anaphylactic reactions 1.8 to 14.4 cases per million doses
- Arthralgias and other joint symptoms 25% (adult women)

MMRV

- Fever of 102°F or higher 21.5%
- Febrile seizures 1 additional per 2,300 to 2,600 children age 12 through 23 months.^[57]

Contraindications:

Allergy

People who experienced a severe allergic reaction (difficulty breathing, hives, hypotension, shock, swelling of the mouth or throat) following a prior dose of MMR or MMRV vaccine, or who had an anaphylactic reaction to topically or systemically administered neomycin, should not be vaccinated or revaccinated. People who are allergic to eggs can receive MMR or MMRV vaccine without prior routine skin testing or the use of special protocols.^[58]



Immunosuppression

Enhanced replication of live vaccine viruses can occur in people who have immune deficiency disorders. Death related to vaccine-associated measles virus infection has been reported among severely immunocompromised people; thus, severely immunosuppressed people should not be vaccinated with MMR or MMRV vaccine. For a thorough discussion of recommendations for immunocompromised travelers.^[58]

HIV

MMR vaccination is recommended for all people with HIV infection aged ≥ 12 months who do not have evidence of measles, mumps, and rubella immunity, and who do not have evidence of severe immunosuppression. The assessment of severe immunosuppression can be based on CD4 values (count or percentage); absence of severe immunosuppression is defined as CD4 $\geq 15\%$ for ≥ 6 months for children aged ≤ 5 years, or CD4 $\geq 15\%$ and CD4 count ≥ 200 cells/mL for ≥ 6 months for people aged 5 years.^[58]

Leukemia

People with leukemia in remission and off chemotherapy, who were not immune to measles when diagnosed with leukemia, may receive MMR vaccine. At least 3 months should elapse after termination of chemotherapy before administering the first dose of vaccine.^[58]

Steroid and other immunosuppressive therapy

Avoid vaccinating people who have received high-dose corticosteroid therapy (in general, considered to be ≥ 20 mg or 2 mg/kg body weight of prednisone, or its equivalent, daily for ≥ 14 days) with MMR or MMRV for ≥ 1 month after cessation of steroid therapy. Corticosteroid therapy usually is not a contraindication when administration is short-term (< 14 days) or a low to moderate dose (< 20 mg of prednisone or equivalent per day).

In general, withhold MMR or MMRV vaccine for ≥ 3 months after cessation of other immunosuppressive therapies and remission of the underlying disease.^[58]

Pregnancy

MMR vaccines should not be administered to pregnant people or people attempting to become pregnant. Because of the theoretical risk to the fetus, people should be counseled to avoid becoming pregnant for 28 days after receiving a live-virus (e.g., MMR) vaccine.^[58]

Precautions

Personal or Family History of Seizures of Any Etiology

Compared with administration of separate MMR and varicella vaccines at the same visit, use of MMRV vaccine is associated with a higher risk for fever and febrile seizures 5–12 days after the first dose among children aged 12–23 months. Approximately one additional febrile seizure occurs for every 2,300–2,600 MMRV vaccine doses administered. Use of separate MMR and varicella vaccines avoids this increased risk for fever and febrile seizures.^[58]

Thrombocytopenia

The benefits of primary immunization are usually greater than the potential risks for vaccine-associated thrombocytopenia. Avoid giving subsequent doses of MMR or MMRV vaccine, however, if an episode of thrombocytopenia occurred ≤ 6 weeks after a previous dose of vaccine.^[58]

Postexposure Prophylaxis

Measles-containing vaccine or immune globulin (IG) can be effective as postexposure prophylaxis. MMR or MMRV administered ≤ 72 hours after initial exposure to measles virus might provide some protection. If the exposure does not result in infection, the vaccine should induce protection against subsequent measles virus infection.^[58]

When administered ≤ 6 days of exposure, IG can be used to confer temporary immunity in a susceptible person. If the exposure does not result in modified or typical measles, vaccination with MMR or MMRV is still necessary to provide long-lasting protection. Six months after receiving intramuscularly administered IG, or 8 months after receiving intravenously administered IG, administer MMR or MMRV vaccine, provided the patient is aged ≥ 12 months and the vaccine is not otherwise contraindicated.^[58]

Giving vitamin A supplementation:

WHO recommended:

(100.000 IU orally) with the first dose of vaccination (at age of 9 months).

(200.000 IU orally) with the second dose of vaccination (at age of 18 months).

The reason:

serum Vit A level reduces significantly 9-14 days after measles vaccine

measles infection depletes the body's stores of Vit A and depress the immune system vit A administration was found to be a potent immune enhancer.^[59]

2.2 WHO STRATEGY PRIORITY

SP1: Primary Health Care and Universal Health Coverage

Include all measles and rubella activities, including surveillance and case management, as key components of PHC systems in support of UHC. Develop and enhance measles and rubella surveillance as part of a comprehensive surveillance system, and improve the collection and use of monitoring and surveillance data.

SP2: Commitment and Demand

Improve ownership and accountability of measles and rubella goals and targets at all levels, and improve community demand for and uptake of measles and rubella-containing vaccines.

SP3: Coverage and Equity

Identify and address measles and rubella immunity gaps at all relevant points of contact between individuals and the health system. Establish or strengthen contact points where needed, and use targeted approaches to reach underserved populations.

SP4: Life Course and Integration

Use the life course approach to deliver the second routine dose of measles and rubella containing vaccines and catch-up vaccination, and integrate measles and rubella activities with other health and non-health activities.

SP5: Outbreaks and Emergencies

Ensure outbreak preparedness for timely detection and effective response to limit the spread of measles and rubella and reduce related morbidity and mortality.

SP6: Supply and Sustainability

Ensure availability of high-quality measles and rubella-containing vaccines, vaccination supplies and laboratory reagents, and ensure that measles and rubella activities, including surveillance, are sustainably financed.

SP7: Research and Innovation

Foster research and innovation to overcome barriers to achieving high measles and rubella population immunity and to generate and use high-quality disease and program data.

Strategic Priority 1

Primary Health Care and Universal Health Coverage

Objective 1

Include all measles and rubella activities, including surveillance and case management, as key components of PHC systems in support of UHC.

Key focus areas

Establish appropriate linkages between vaccination and other health interventions to work towards achieving UHC. Planning and delivery of measles- and rubella-containing vaccines must be linked to the delivery of other scheduled vaccinations and health interventions, in order to improve efficiencies. Close collaboration and cohesive action among all relevant programs should be fostered to improve the uptake of each intervention.

Use measles outbreaks as the trigger for action to improve universal access to a minimum package of health interventions. Measles outbreaks serve to highlight communities that lack access to basic health services and can be markers of inequity in health service delivery. They can serve as the trigger for implementing tailored interventions in and beyond immunization as well as efforts to identify where system strengthening is needed. Outbreak response should include root cause analysis to define the reasons for immunity gaps, with plans for sustainable remedial actions to promote the reintegration of immunization into the PHC system where required. Outbreak response must also be holistic, including appropriate case management and nutritional support.

Objective 2

Develop and enhance measles and rubella surveillance as part of a comprehensive surveillance system, and improve the collection and use of monitoring and surveillance data for action.

Key focus areas

Strengthen comprehensive surveillance systems. Surveillance is an essential component of measles and rubella elimination and of immunization programs in general. Data on measles cases, including geographic and age distribution, can highlight immunity gaps that are not identified by monitoring of vaccination coverage alone. Surveillance data can also help guide effective operational planning. As the number of disease control programs increases, it is important to pivot away from fragmented, vertical and unsustainable surveillance structures. Collaboration across different disease programs to establish shared governance mechanisms, strengthen national capacity for surveillance, and share laboratory networks and quality control processes will lead to a more efficient, sustainable and comprehensive surveillance system.

Strengthening comprehensive surveillance systems to meet elimination standards will also improve the ability to prevent, detect and control outbreaks of measles and other diseases in a timely manner. While sustainable surveillance that meets established standards is primarily the responsibility of national governments, technical support and coordination at the regional and global levels are essential for quality assurance and data sharing. This includes maintaining and enhancing the support provided through the Global Measles and Rubella Laboratory Network.

Measles and rubella surveillance activities that were interrupted as a result of the COVID-19 pandemic should be re-established as quickly as possible. Case detection, investigation and contact tracing capabilities established in response to the pandemic should be applied to further strengthen surveillance systems.

The availability of high-quality monitoring data at all administrative levels is essential for monitoring programme performance, identifying gaps and informing operational decisions to achieve measles and rubella elimination and control. Renewed efforts are required to improve the quality of data in accordance with recent recommendations.^[60]

Strategic Priority 2

Commitment and Demand

Objective

Improve ownership and accountability of measles and rubella goals and targets at all levels, and improve community demand for and uptake of measles and rubella-containing vaccines.

Key focus areas

Conduct regular assessment of progress against measles and rubella goals, targets and milestones, and establish accountability processes. Commitment by national governments and all key stakeholders to the global, regional and national measles and rubella goals, targets and milestones are critical to success. Commitment is demonstrated through regular assessment of progress against the relevant indicators, accountability for achieving relevant targets and milestones, and allocation of adequate resources to achieve targets.

Strengthen and sustain political will to achieve measles and rubella goals. Political will and leadership are critical to success. All stakeholders should work collectively to strengthen and sustain political will and the commitment of global, regional and national leaders to achieving measles and rubella elimination goals.

Strengthen national and subnational capacity for community engagement, demand creation and risk communication. Countries should apply lessons learned from other efforts and use both traditional and modern communication and demand creation strategies and techniques to enhance trust and improve the uptake of measles- and rubella-containing vaccines.^[60]

Strategic Priority 3

Coverage and Equity

Objective

Identify and close measles and rubella immunity gaps by using all relevant points of contact between individuals and the health system. Establish or strengthen contact points where needed, and use targeted approaches to reach underserved populations.

Key focus areas

Promote integrated service delivery to achieve and maintain high coverage of two doses of measles- and rubella-containing vaccines. Routine delivery of immunization services integrated with other scheduled child health interventions must become the standard for achieving and maintaining high population immunity. Such an approach will provide opportunities for joint actions to improve coverage and strengthen the 2YL platform. In situations where routine services have been interrupted for an undetermined period (such as during the COVID-19 pandemic), children who miss their scheduled doses of vaccination should be carefully monitored and strategies should be developed to provide catch-up vaccination.

Identify and plan gender-responsive interventions to ensure that vulnerable populations (such as migrants and nomadic, socially marginalized, urban poor, indigenous and conflict-affected populations) are vaccinated.

This includes ensuring equity-based policies and adequate financing to support vaccination in fragile countries and among vulnerable populations and ensuring inclusion of the latter in national immunization plans. Different delivery approaches will need to be explored, such as outreach and differentiated delivery strategies for special populations as well as periodic intensification of routine immunization (PIRI) services. The sustainability of these approaches will be crucial to long-term success.

Identify and close immunity gaps through supplementary mean of vaccine delivery. The need for supplementary means to fill immunity gaps, especially in populations without access to routine service delivery, is well recognized. In strategic shift, tailored approaches should be used rather than sole reliance on nonselective mass campaigns. These tailored approaches should use surveillance, immunization coverage and geospatial mapping data to target those missed by routine services and to deliver routine vaccine doses (such as through PIRI) or supplementary doses such as through SIAs). These approaches should include special efforts to bring the “missed” individuals within the ambit of routine service delivery and strengthen health systems to sustainably deliver all PHC services to their communities. In the early part of the decade and due to the COVID-19 pandemic, a combination of PIRI and SIAs will likely be required in many countries to fill immunity gaps because of missed routine vaccination doses and the cancellation of planned SIAs.

Promote integrated delivery of vaccines and non-vaccine preventive interventions in preventive campaigns to create efficiencies and maximize impact. Where indicated and feasible, joint campaigns that combine preventive vaccination with other disease initiatives such as for polio, yellow fever, cholera or meningococcal meningitis vaccination(or take place during World Immunization Week campaigns should be implemented. Where appropriate and feasible, other non-vaccine preventive interventions (such as vitamin A supplementation) may be included in such campaigns.^[60]

Strategic Priority 4

Life Course and Integration

Objective

Use the life course approach to deliver the second routine dose of measles and rubella-containing vaccines and catch-up vaccination, and integrate measles and rubella activities with other health and non-health activities.

Key focus areas

Use the life course approach for catch-up measles and rubella vaccination.

Catch-up vaccination will continue to be required for those who missed their two routine doses of measles and rubella-containing vaccines. The increasing focus on life course vaccination, especially at school age, in adolescence and in adulthood will catalysis efforts to mainstream catch-up vaccination and reduce the frequency and scale of SIAs to fill immunity gaps.

Review country policies. Country policies on vaccination (such as vaccination eligibility criteria, day care or school vaccination checks, and vaccination of health workers and travelers) will need review, discussion and revision to ensure that they enable the life course approach and facilitate integration.

Establish coordination mechanisms. Governance structures and coordination mechanisms that facilitate joint programming, promote integration between different health programs and foster intersect oral collaboration (such as between the health and education sectors or the public and private health sectors) should be strengthened or established to facilitate life course vaccination.^[60]

Strategic Priority 5

Outbreaks and Emergencies

Objective

Ensure outbreak preparedness for timely detection and effective response to limit the spread of measles and rubella and reduce related morbidity and mortality.

Key focus areas

Develop stronger linkages between measles and rubella elimination and control efforts and the international health regulations and related processes. This should include the use of the joint external evaluation process to assess and strengthen country capacity to prevent, detect and rapidly respond to measles and rubella outbreaks and promote the inclusion of measles and rubella in national action plans for health security.

Strengthen national and subnational capacity for outbreak preparedness and response in collaboration with other disease programs. The various national programs (such as epidemiology, immunization, and humanitarian and emergency response programs) and partners should work in close coordination, share resources and responsibilities, and jointly support national capacity strengthening for outbreak preparedness, detection, investigation and response, including case management and nutritional support for measles.

Harness the expertise of CSOs. CSOs with experience operating in areas outside the reach of national governments or international agencies have valuable expertise that can help with preparing and responding to outbreaks and humanitarian emergencies. Collaboration and partnership with CSOs are especially crucial for emergency and outbreak response in countries experiencing protracted conflicts.

Strengthen capacity for outbreak investigations to identify root causes of outbreaks and inform corrective actions to improve health systems and routine immunization programs. An outbreak of measles indicates an immunity gap. Outbreak investigations are needed to identify the root causes, identify chains of transmission and use the resulting information to improve and strengthen the health and immunization systems.

Improve structures and processes to support countries in responding to outbreaks in a timely and effective way. Provide greater clarity on the need, scope and timelines for an optimal response to measles and rubella outbreaks with vaccination. Streamline global and regional structures and processes, such as through sharing of human resources to conduct epidemiological analyses, assisting with campaign planning and implementation, and conducting monitoring activities during and after campaigns.

Improve cross-border collaborations to mitigate the spread of measles and rubella. Cross-border populations are often not included in immunization micro plans, which can lead to immunity gaps in those communities. Population movement across borders also increases the risk of importation and spread of outbreaks between neighboring countries. Increased monitoring of immunization status, timely data sharing and joint action in border areas can reduce immunity gaps in cross-border communities and mitigate the risk of outbreaks.^[60]

Strategic Priority 6

Supply and Sustainability

Objective

Ensure availability of high-quality measles- and rubella-containing vaccines, vaccination supplies and laboratory reagents, and ensure that measles and rubella activities, including surveillance, are sustainably financed.

Key focus areas

Ensure the timely availability of sufficient vaccine supplies and laboratory reagents and consumables. The right products in the right presentations and at affordable prices are necessary to meet country and community needs for planned routine vaccination as well as planned and unplanned supplemental immunization and outbreak response. National governments, vaccine manufacturers and global partners should continue collaborating to ensure vaccine security and improve the health of the supply market for vaccines, supplies and laboratory reagents of assured quality.

Ensure sufficient financing for all measles and rubella activities, including surveillance, within health planning and budgeting at all levels. Regular planning and budgeting for measles and rubella activities as part of overall immunization and health planning and budgeting is necessary, together with coordination and advocacy mechanisms to ensure that sustainable funding is available to achieve measles and rubella goals and targets.

Ensure financing for fragile areas or countries. Sustainable external financial support for conflict-affected and fragile countries is necessary, via existing mechanisms (such as GAVI) or new mechanisms, as well as financing at the global and regional levels for coordination, technical support and monitoring.^[60]

Strategic Priority 7

Research and Innovation

Objective

Foster research and innovation to overcome barriers to achieving high measles and rubella population immunity and to generate and use high-quality disease and programme data.

Key focus areas

Conduct formative research. Formative research can provide insights and information to help tailor immunization services to address health system barriers, improve the uptake of vaccination, and document best practices for outbreak control. Lessons learned from operational and behavioral research can be used to tailor activities for different contexts and communities.

Develop and fund innovative vaccine delivery platforms and technologies. Innovations such as microarray patches for vaccination can enable delivery of immunization services with fewer human resources, especially to underserved populations during SIAs and for outbreak response. Discovery, development and use of new technologies to reach such populations should be promoted to accelerate progress towards disease elimination.

Explore, evaluate and scale up the use of innovative service delivery strategies. Achieving the high levels of vaccination required to interrupt transmission of measles requires new strategies to vaccinate underserved populations and people residing in areas of civil unrest or insecurity. Innovative strategies should be evaluated when developing best practice guidelines for vaccinating such populations.^[60]

2.3 EPIDEMIOLOGY

Overview

Being vaccinated is the best way to prevent getting sick with measles or spreading it to other people. The vaccine is safe and helps your body fight off the virus.

Before the introduction of measles vaccine in 1963 and widespread vaccination, major epidemics occurred approximately every two to three years and caused an estimated 2.6 million deaths each year.

An estimated 128,000 people died from measles in 2021 – mostly children under the age of five years, despite the availability of a safe and cost-effective vaccine.

Accelerated immunization activities by countries, WHO, the Measles & Rubella Partnership (formerly the Measles & Rubella Initiative), and other international partners successfully prevented 56 million deaths between 2000–2021. Vaccination decreased measles deaths from 761000 in 2000 to 128 000 in 2021.^[68]

Age-related demographics

Although measles is historically a disease of childhood, infection can occur in unvaccinated or partially vaccinated individuals of any age or in those with compromised immunity.

Unvaccinated young children are at the highest risk. Age-specific attack rates may be highest in susceptible infants younger than 12 months, school-aged children, or young adults, depending on local immunization practices and incidence of the disease. Complications such as otitis media, bronchopneumonia, laryngotracheobronchitis (croup), and diarrhea are more common in young children. In heavily populated, underdeveloped countries, measles is most common in children younger than 2 years.^[61]

The average age at measles infection depends on the age at which maternal antibody is lost and on age-related changes in frequency of contact with other persons. Measles occurs among younger children in developing than industrialized countries because of the higher birth rates, more crowded living conditions, and earlier loss of maternal antibody in the former (BLACK et al. 1986). Similarly, the age at infection is earlier in urban than rural areas. The average age of infection was 4-6 years in most industrialized countries in the early 1960s, prior to the introduction of widespread immunization (WALSH 1983). In Senegal, 100% of urban children were seropositive at 18-24 months of age, whereas in rural areas 100% seropositivity was not reached until 10 years of age (BOUE 1964).^[62]

Sex- and race-related demographics

Unvaccinated males and females are equally susceptible to infection by the measles virus. Excess mortality following acute measles has been observed among females at all ages, but it is most marked in adolescents and young adults. Excessive non-measles-related mortality has also been observed among female recipients of high-titer measles vaccines in Senegal, Guinea Bissau, and Haiti.^[63]

Measles affects people of all race.

The epidemiological situation of measles in Yemen

The epidemiological situation of measles in Yemen has been a significant public health concern. Before 2006, measles was considered the fourth leading cause of death among children under five years old, according to a health survey conducted by the Family Health Survey in 2003. Prior to 2006, the World Health Organization estimated approximately 30,000 measles cases and around 5,000 measles-related deaths in Yemen annually.

The year 2006 marked a significant turning point in the efforts to eliminate measles in Yemen. The country conducted its first nationwide catch-up immunization campaign targeting children aged 9 months to 15 years, reaching approximately 9 million children with a high coverage rate of 98%, as confirmed by independent monitoring reports. Measles cases decreased significantly following this nationwide campaign, with 13,555 cases reported in 2007 and 2008. In line with the strategies to eliminate measles, subsequent nationwide immunization campaigns were implemented in 2009 and 2012 to enhance immunity and prevent the accumulation of susceptible children. However, due to low coverage in some areas for routine vaccination and campaigns, the incidence of measles increased in 2011 and 2012.

In 2006, there were 321 confirmed cases with an infection rate of 55 cases per million of the population.

A national campaign targeting children aged 9 months to 15 years was implemented.

In the following years:

- In 2007, the required data was not provided.
- In 2008, the required data was not provided.
- In 2009, the required data was not provided.
- In 2010, there were 26 cases with an infection rate of 127 cases per million of the population. A national campaign targeting children aged 9 months to 5 years was implemented.
- In 2011, there were 2632 cases with an infection rate of 2168 cases per million of the population. A national campaign targeting children aged 9 months to 10 years was implemented.

- In November 2014, a national campaign targeting children aged 9 months to 15 years was implemented. The specific data was not provided.
- In 2018, an emergency mini-campaign was conducted in 38 directorates, and 29 cases were recorded.
- In 2021, there were 1179 cases recorded. Details about the campaigns implemented in that year were not provided.^[64]

International statistics

In developing countries, measles affects 30 million children a year and causes 1 million deaths. Measles causes 15,000-60,000 cases of blindness per year.

In 1998, the cases of measles per 100,000 total population reported to the World Health Organization (WHO) was 1.6 in the Americas, 8.2 in Europe, 11.1 in the Eastern Mediterranean region, 4.2 in South East Asia, 5.0 in the Western Pacific region, and 61.7 in Africa. In 2006, only 187 confirmed cases were reported in the Western Hemisphere (mainly in Venezuela, Mexico, and the United States).

Between 2000 and 2008, the number of worldwide measles cases reported to the WHO and the United Nations Children's Fund (UNICEF) declined by 67% (from 852,937 to 278,358). During the same 8-year period, global measles mortality dropped by 78%. However, it is believed that global measles incidence and mortality remain underreported, with many countries, particularly those with the highest disease burden, lacking complete, reliable surveillance data.

Since 2008, France has been experiencing an outbreak of measles, which has not yet begun to slacken. Over the same period, outbreaks have also been occurring in the 46 countries of the WHO African Region. Worldwide, most reported cases of measles continue to be from Africa.^[63]

Measles Outbreak in Egypt in 1974:

In 1974, Egypt experienced a measles outbreak. This outbreak was one of the largest and most severe epidemics the country faced during that period. Cases of measles were documented in several regions of Egypt, with densely populated areas being particularly affected.

The Egyptian authorities dealt with the measles outbreak in 1974 by implementing various preventive and treatment measures. Wide-scale vaccination campaigns were conducted in the affected areas, providing measles vaccines to both children and adults. Guidance and awareness efforts were also provided to the community regarding the symptoms and modes of measles transmission, as well as the importance of vaccination.

Efforts were coordinated between the Ministry of Health, local health authorities, and civil society organizations to effectively respond to the outbreak. Enhanced health surveillance and active monitoring were implemented to track and record the affected cases, while infected individuals were isolated to minimize the spread of the disease. Hospitals and healthcare centers were equipped with the necessary equipment and supplies to treat the infected individuals and provide them with the required care.^[65]

Several preventive measures have been implemented in Egypt to combat the measles epidemic. These measures include:

Vaccination campaigns:

Wide-scale vaccination campaigns were organized to provide measles vaccines to children and adults in affected areas. These campaigns aim to increase vaccination rates and achieve herd immunity to reduce the spread of the disease.

Health awareness:

Guidance and awareness were provided to the community regarding measles symptoms, transmission methods, and the importance of vaccination. This includes distributing educational and awareness materials and conducting mass communication efforts to disseminate accurate health information.

Active immunization:

Health surveillance and active monitoring were strengthened to detect measles cases and isolate infected individuals to prevent the spread of the infection. These efforts involve collaboration with healthcare institutions, hospitals, and doctors to identify cases and provide necessary care.

Training and development:

Professional training and development for healthcare workers were enhanced to increase awareness and competence in dealing with the measles epidemic. These efforts included providing information and technical and scientific training for healthcare personnel.^[66]

Has success been achieved in implementing these measures in Egypt?

Yes, significant success has been achieved in implementing the preventive measures for the measles epidemic in Egypt. Over time, the number of measles cases has declined, and the spread rates have decreased, reflecting the effectiveness of the implemented measures and the efforts of the authorities and relevant entities.

Wide-scale vaccination campaigns were carried out to increase vaccination rates and achieve herd immunity. Through these campaigns, vaccines were provided to children and adults in affected areas, contributing to reducing the spread of the disease.

Health surveillance and active monitoring were strengthened to detect cases of infection and isolate the affected individuals to prevent transmission. Thanks to these efforts, infected cases were identified, and necessary measures were taken to control the spread of the disease.

Additionally, health awareness was enhanced, and accurate information was provided to the community, contributing to increased awareness of measles symptoms, transmission methods, and the importance of vaccination.

After the implementation of preventive and treatment measures, the Egyptian authorities succeeded in controlling the measles epidemic in Egypt in 1974. Vaccines were made available, and wide-scale vaccination campaigns were carried out, leading to increased vaccination rates and reduced disease spread. Health surveillance and active monitoring were enhanced to detect cases of infection and isolate the affected individuals to prevent transmission.

Subsequently, a decrease in the number of measles cases and spread rates was observed. These results reflect the effectiveness of the measures taken and the efforts of the authorities in addressing the epidemic.

However, it is important to note that maintaining awareness and continuous efforts in vaccination and health surveillance are crucial to prevent future outbreaks of measles. Disease outbreaks can reoccur if vaccination rates decrease or if there is a lack of health awareness in the community.^[67]

Measles Outbreak in Yemen in 2011:

The measles epidemic in Yemen in 2011 was a severe outbreak that led to the spread of measles in various regions of the country. According to available information, Yemen suffered

from low vaccination coverage and a weak healthcare infrastructure, which contributed to the rapid spread of measles in the country.

Reports from the World Health Organization and non-governmental organizations indicated that measles was significantly impacted by the armed conflict in Yemen, as healthcare efforts were disrupted and the healthcare infrastructure deteriorated, leading to a decline in vaccination coverage and an increase in the number of cases.

Estimates of measles cases in Yemen in 2011 vary depending on different sources. According to reports from the World Health Organization, there were over 25,000 reported cases and more than 200 deaths due to measles in that year. Young children were the most affected by the disease.

Sana'a, 5 March 2012 (IRIN) - Measles has killed 126 children in Yemen since mid-2011, a consequence of the breakdown of basic health services during the year-long political crisis. In response to the big increase in reported cases and deaths due to measles, the Yemeni government has appealed for international assistance and an outbreak-response vaccination campaign will begin in the hardest-hit regions on 10 March.

"It's very sad that we were talking about elimination in 2010, and now we are dealing with an outbreak," said Arwa Baider, a child health program officer at the UN Children's Fund (UNICEF).

The latest statistics from the Health Ministry at the end of February report that 3,767 cases of measles have been confirmed, resulting in 126 deaths, since mid-2011. By comparison, in the three years from the beginning of 2007 until the end of 2009, the ministry reported a total of 211 cases and no deaths due to measles.

Seventy percent of these cases, and all of the deaths, were among children under five years of age. Most of the cases and deaths have occurred in the last four months. Measles has been reported across the country, but has been concentrated in Abyan, Aden, Al Bayda, Shabwa, Dhamar, Lahj, Amran and Sa'adah governorates.

"The disease is spreading fast, reaching highly populated areas as well as areas with high levels of acute malnutrition," Geert Cappelaere, a representative of UNICEF in Yemen, told IRIN.

"There is a very valid concern of many more deaths if a massive country-wide immunization campaign is not started immediately."

According to the World Health Organization (WHO), measles outbreaks can be particularly deadly in countries recovering from conflict. Damage to health infrastructure and health services interrupts routine immunization, and overcrowding in residential camps increases the risk of infection.

"The outbreak is a direct result of a decrease in routine immunization services during 2011; which is a direct result of the 2011 conflicts," added Cappelaere.

In conflict-affected areas doctors reported being unable to deliver vaccinations because they were stopped at checkpoints, short of staff, or the refrigerated vaccines spoiled due to electricity cuts. In July 2011, WHO reported that fuel shortages had disrupted the cold chain supply system, resulting in the closure of 30 percent of immunization facilities.

Immunization rates also decreased in some areas, such as Abyan, due to a "resurgence of radical religious views - negative views - about vaccination," said the Ministry of Health's director-general of family health, "Radical religious groups say that vaccination is not needed, it's against God's will and so on. Some communities believe this and started to resist or not accept vaccination. This is one of the reasons why in those areas we see pockets of lower vaccination coverage."

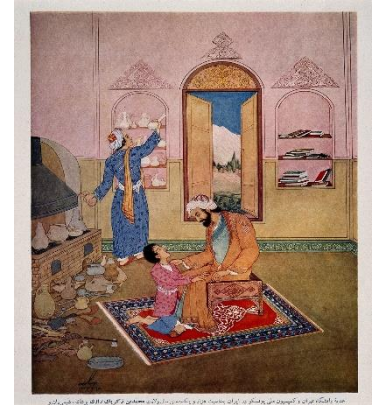
In Yemen, the measles crisis is more acute because of the country's high levels of malnutrition. Severe measles is more likely to develop among poorly nourished children; whose weakened immunity leaves them vulnerable to the complications caused by measles. According to UNICEF, 58% of Yemeni children are stunted and are chronically malnourished - the second highest rate in the world after Afghanistan. In the worst-affected parts of the country, 30 percent of children suffer from acute malnutrition, a level twice as high as the internationally recognized emergency threshold, and on a par with parts of southern Somalia.

In response to the measles outbreaks, UNICEF in partnership with the Ministry of Health, WHO, and the US Agency for International Development, will launch the first phase of an outbreak-response vaccination campaign on 10 March in seven of the worst-affected governorates: Abyan, Aden, Lahj, Shabwa, Dahmar, Al Bayda, and Sa'adah. The second phase of the campaign will broaden vaccination across the country, but is dependent on additional funding.^[68]

2.4 GLOBAL HISTORY OF MEASLES

History of measles

The Persian physician Rhazes gave the first clinical description of the disease in the 10th century, clearly differentiating it from smallpox. Measles spread worldwide from the Renaissance. Its epidemiology was remarkably studied in 1846 by a Danish physician, Peter Panum, during an epidemic in the Faroe Islands. The viral nature of this disease was demonstrated in 1911 and the virus was identified in 1954 by Thomas Peebles and John Enders. It is a morbillivirus (family Paramyxoviridae), also a responsible for rinderpest (ovine, bovine), distemper (canine, feline), and epidemic diseases of dolphins, porpoises and seals. The current measles virus appeared recently from the rinderpest virus around the 6th century BCE. It has adapted perfectly to the human species, becoming strictly human, without animal reservoirs. A live attenuated vaccine was developed in 1958 by Enders' team after numerous passages in cell cultures. The vaccine was licensed in the United States in 1963 and is used on a large scale by the WHO throughout the world. This highly effective and well-tolerated vaccine has greatly reduced the number of measles cases and saved millions of lives. Measles remains a major public health concern, causing over 100,000 deaths per year worldwide. Today, the most affected continents remain Africa, South America and Asia.^[70]



Pre-vaccine era

In the 9th century, a Persian doctor published one of the first written accounts of measles disease.

Francis Home, a Scottish physician, demonstrated in 1757 that measles is caused by an infectious agent in the blood of patients.

In 1912, measles became a nationally notifiable disease in the United States, requiring U.S. healthcare providers and laboratories to report all diagnosed cases. In the first decade of reporting, an average of 6,000 measles-related deaths were reported each year.

In the decade before 1963 when a vaccine became available, nearly all children got measles by the time they were 15 years of age. It is estimated 3 to 4 million people in the United States were infected each year. Also, each year, among reported cases, an estimated 400 to 500 people died, 48,000 were hospitalized, and 1,000 suffered encephalitis (swelling of the brain) from measles.^[71]

Vaccine development

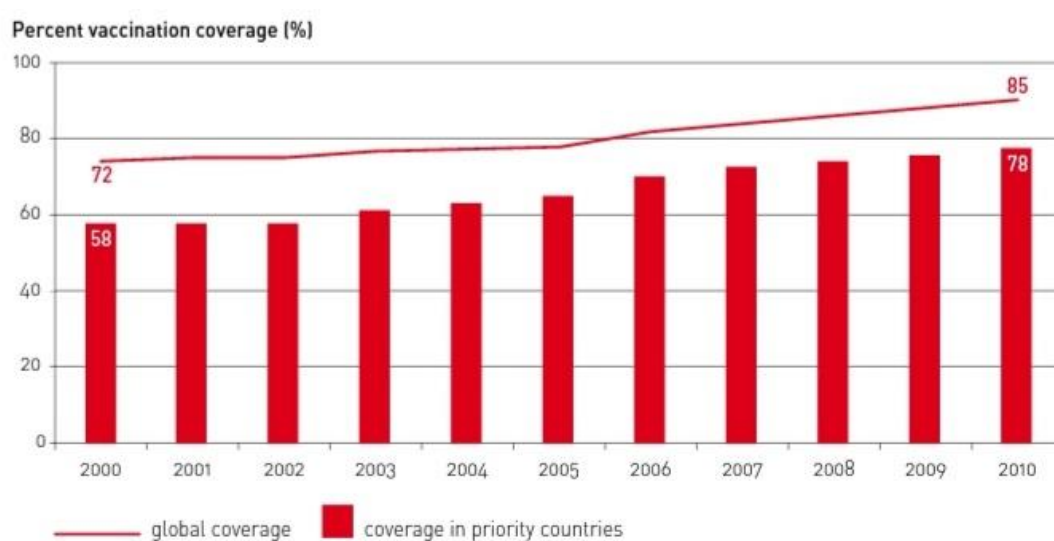
In 1954, John F. Enders and Dr. Thomas C. Peebles collected blood samples from several ill students during a measles outbreak in Boston, Massachusetts. They wanted to isolate the measles virus in the student's blood and create a measles vaccine. They succeeded in isolating measles in 13-year-old David Edmonston's blood.

In 1963, John Enders and colleagues transformed their Edmonston-B strain of measles virus into a vaccine and licensed it in the United States. In 1968, an improved and even weaker measles vaccine, developed by Maurice Hilleman and colleagues, began to be distributed. This vaccine, called the Edmonston-Enders (formerly "Morten") strain has been the only measles vaccine used in the United States since 1968. Measles vaccine is usually combined with mumps and rubella (MMR), or combined with mumps, rubella and varicella (MMRV). Learn more about measles vaccine.^[71]

Despite the availability of a safe, heat-stable, effective and inexpensive measles vaccine, and the substantial progress towards measles control, measles remains one of the leading causes of preventable death globally among children. In 2000, the World Health Assembly adopted a resolution to reduce global measles deaths by half compared with 1999 levels, from 2000–2005.

This goal was achieved globally following the implementation of a five-year strategic plan to increase coverage with measles vaccination through routine immunization and SIAs. Concurrently, the delivery of other safe, effective and affordable child-survival health interventions was scaled up (such as combining measles vaccine with vitamin A supplementation, deworming medicine, insecticide-treated bed nets and polio vaccine) in the highest burden countries. The targeted countries supported the strategy with strong political commitment. Following this achievement, the MR Initiative supported a five-year strategic plan in 2006 with a more ambitious goal to reduce estimated measles mortality by 90% by 2010 compared with 2000 levels. Considerable progress was achieved by 2010: about 9.6 million deaths were averted by measles immunization during 2000–2010 including routine and SIAs, and with the exception of the South-East Asia Region, all WHO regions have achieved at least 75% reduction in measles mortality in 2010 compared to 2000. The 90% measles mortality reduction goal was not achieved mainly due to delayed implementation of measles control activities in India and large-scale measles outbreaks in Africa. By 2011, all 194 WHO Member States had introduced or begun the process of introducing a two-dose measles vaccination strategy delivered through routine immunization services and/ or SIAs. According to WHO and UNICEF estimates, global routine

coverage with a first dose of measles vaccine (MCV1) increased from 72% in 2000 to 85% in 2010 (Figure18). During this same period, coverage increased from 58% to 78% in the 47 countries with the highest burden of measles. By the end of 2010, the routine immunization schedules of 139 countries included two doses of measles-containing vaccine (MCV), and in 2011, GAVI supported 11 more countries to introduce a routine second dose of measles (MCV2). The timing of MCV2 serves as an important contact between the child and the Expanded Programme on Immunization (EPI) because it provides an opportunity to catch up on any missed vaccinations and deliver boosters, e.g. diphtheria-tetanus-pertussis (DTP) vaccine to older age groups.^[72]



(Figure18): *1st Dose Measles Coverage Globally and in 47 Measles Priority Countries 2000-2010.* ^[73]

Measles elimination

In 1978, CDC set a goal to eliminate measles from the United States by 1982. Although this goal was not met, widespread use of measles vaccine drastically reduced the disease rates. By 1981, the number of reported measles cases was 80% less compared with the previous year. However, a 1989 measles outbreaks among vaccinated school-aged children prompted the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP) to recommend a second dose of MMR vaccine for all children. Following widespread implementation of this recommendation and improvements in first-dose MMR vaccine coverage, reported measles cases declined even more.

Measles was declared eliminated (absence of continuous disease transmission for greater than 12 months) from the United States in 2000. This was thanks to a highly effective vaccination program in the United States, as well as better measles control in the Americas region.^[74]

Global Considerations

Remarkable progress has been made in reducing global measles incidence and mortality rates through measles vaccination. In the Americas, intensive vaccination and surveillance efforts based in part on the successful Pan American Health Organization strategy of periodic nationwide measles vaccination campaigns (supplementary immunization activities, or SIAs) and high levels of routine measles vaccine coverage interrupted endemic transmission of measles virus.

The World Health Organization's (WHO's) Region of the Americas was declared to have eliminated measles in September 2016 the first region in the world to do so.

In the United States, high level coverage with two doses of measles vaccine eliminated endemic measles virus transmission in 2000. More recently, progress has been made in reducing measles incidence and mortality rates in sub-Saharan Africa and Asia as a consequence of increasing routine measles vaccine coverage and provision of a second dose of measles vaccine through mass measles vaccination campaigns and childhood immunization programs.

In 2003, the World Health Assembly endorsed a resolution urging member countries to reduce the number of deaths attributed to measles by 50% (compared with 1999 estimates) by the end of 2005. This target was met.

Global measles mortality continued to decline and, by 2015, there were an estimated 134,200 deaths due to measles (uncertainty bounds: 74,400 and 353,600 deaths).

These achievements attest to the enormous public-health significance of measles vaccination. However, recent large outbreaks of measles in Europe and Africa illustrate the challenges faced in sustaining measles control: in these outbreaks, measles was imported into countries that had eliminated indigenous transmission of measles virus.

Through its 2012–2020 Global Measles and Rubella Strategic Plan, the Initiative aimed to reduce measles deaths by 95% (compared with year 2000 estimates) by 2015 and to eliminate measles from at least five of the six WHO regions by 2020.^[75]

2.5 HISTORY OF MEASLES IN YEMEN

Measles is a highly infectious vaccine-preventable disease and leading cause of death among children.

In Yemen, measles cases were reported during 1989–2002.

Measles is still a global threat especially among children were 355,000 cases and 1581000 deaths were reported in 2011. In Yemen, measles incidence rates have increased from three per 100,000 populations in 2008 to 13 in 2011. The Measles Surveillance System (MSP) was established in 2007 to predict epidemics and monitor progress towards eradication. The aim is to assess the MSP usefulness and evaluate performance according to its attributes.^[76]

Prior to 2011, measles was at elimination phase in Yemen however, as vaccination coverage dropped to 71% due to political unrest several outbreaks reported. In May 2012, Qufl Shamr district, Hajjah governorate reported sudden increase of cases of fever and rash.

This is the first measles outbreak in Yemen with high fatality rate. All deaths were unvaccinated and most confirmed cases from area where no vaccination services or vitamin A are provided.

Sixty cases fulfill the case definition with mean age of 6 and male to female ratio of 1:2. Common symptoms were fever (100%), rash (68%), difficulty breathing (32%) and diarrhea (30%). Hemorrhagic manifestation and mouth ulcers present in 20%. Measles IgM was positive in 12 cases. Vaccine coverage among confirmed cases was 5% compared to 46% among non-confirmed (P-value =0.0006). Seven deaths (71%) reported among under-five children with case fatality of 12%. All deaths were from Alholog village and unvaccinated. Out of seven deaths, four were epidemiologically linked to confirmed cases.^[77]

In 2012, a large measles outbreak occurred in Sa'adah governorate. The measles vaccine coverage among children aged 9–18 months varied widely (27% –49 %) between 2009 and 2010. In June 2004, violent conflict took place in Sa'adah, where many people lost their lives and 250,000 people were displaced. In May 2008, it was estimated that 77,000 internally displaced persons (IDPs) were in Sa'adah as a result of the conflict.

The outbreak affected all Sa'adah governorate. Vaccination campaigns were conducted in Sa'adah governorate in April, 2012 to control the increasing cases of measles. Of the 804 reported measles cases, 445 (55%) were males; 359 (45%) were females. One hundred twenty (15%) were laboratory confirmed and 684 (85%) were epidemiologically linked cases. The age groups that were affected mostly were children 3-15 year of age (n=362, 45%) and ≤ 1 year old (n=345, 43%). Among the 362 children 3-15 year of age, 190(52%) were boys and 172 (48 %) were girls. The attack rate was $(804/219563 = 36.6\%)$. There were 505 hospitalizations and 15 deaths., this outbreak was caused by an imported measles into the displaced population of children, whose parents had refused to have them vaccinated because of vaccine safety concerns.^[78]

In mid-February 2015, the surveillance coordinators in Al Matamma and Al Matoon districts at Al Jawf Governorates reported an increased number of fever cases with skin rash suspected as a measles case. Al Jawf Governorate is one of the remote northern governorates that suffers from fragmented power structures and overall instability. A total of 93 cases were reported from 1st January to March 17, 2015. Mostly cases reported within February and March 2015 with the peak in week 10. Two third of Al Jawf districts were affected with case fatality rate 2%. The disease is more prevalent among males than females (1.4:1.0) and around two thirds of cases below 5 years. All cases had fever and rash, 78% had conjunctivitis, 71% had cough and 38% had runny nose. 84% of cases were among unvaccinated children. Among those who were partially vaccinated, two thirds were vaccinated only during campaigns and all of them received only first dose of measles vaccine, 33 cases (72%) of found to be IgM positive large measles outbreak has been confirmed in two thirds of districts at Al Jawf governorate mainly among un-vaccinated children due to parent's refusal.^[79]

On October 12, 2014, the surveillance coordinator in Al Tuhita district notified about 17 suspected measles cases with eight deaths at Al Zelihah village. On 2 November, a team sent for further investigation of the outbreak. Seventy-four cases reported from 29th September to 6th November 2014. All cases were unvaccinated due to documented parents' refusal. The attack rate was 15/100 population with a case fatality rate of 16%. 51% were males and 84% were children 10 years. Out of the 18 blood samples collected, 15 (83%) were IgM positive. Four cases needed admission due to the severe complication where two cases had pneumonia, one had blindness, and one had meningoencephalopathy.^[80]

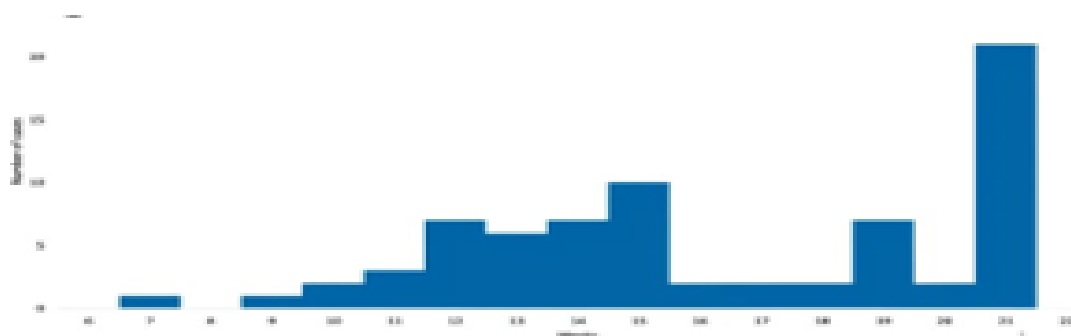
In Ibb-Yemen, 2014 Out of 511 suspected measles cases that were reported from 1st January-30th October 2014, 30 cases (6%) met probable case definition with an incidence rate of 11.5/1,000,000. 53% was among <5 years' age group and 40% among 5-10 years with females representing 53%. 70% of cases were vaccinated against measles of which 50% received 2 two doses. All cases had fever and skin rash but cough, runny nose and conjunctivitis were reported in 58%, 51% and 46% of cases respectively. 20 (67%) has positive IgM for measles and 7 (35%) positive for both measles and rubella IgM incidence among vaccinated children^[81].

During January and February 2015, the surveillance coordinators of Sa'adah governorate noted an increased number of fever cases with skin rash suspected as a measles cases- On March 4 The (MoPHP) send a team of FETP to field to investigate the problem.

A total of 260 cases were reported from December 31, 2014 to March 8, 2015. The most cases reported in the second half of January and February 2015 and the peak of epi curve was at week 7. Two third (11 districts) of Sa'adah districts were affected where most cases were from Razih (28%), Qataber (22%) and Sahar (13%) - 70% of cases were between (1 - 5) years old, 23% were below 1 year and 58% among males. 97% of cases were unvaccinated. 13 blood samples were collected for lab confirmation using Elisa, 12 cases (92%) of them were IgM positive, 1 case (8%) negative. Measles outbreak was confirmed in Sa'adah where very low immunization cover: age and a weak community awareness played a major role.^[82]

On 3 March, 2017, cases with fever and skin rash were reported in Khywan, Huth district, Amran by electronic disease early warning system (eDEWS) coordinator. A team from Y-FETP was sent to investigate the problem. Thirty-two cases met the standard case definition, the index case was reported in 5 Feb. 2017, the outbreak continued till 5 March with the peak of cases in 3 March 2017 (6 cases). The percentage of females was 53%. The highest percent was among the age group 1-< 5 years with the attack rate 21/1000 of population. The percent of non-vaccinated cases was 97%. Reasons for non – vaccination were: lack of outreach vaccination services (39%), absence of vaccine in the nearby health center (39%), and vaccination refusal (22%). All cases had fever and skin rash, 97% of cases had cough and conjunctivitis. About 13% of cases were admitted in Huth hospital due to pneumonia as a complication of measles.^[83]

On May 22, 2018, the surveillance officer in Shabwa governorate reported an increased number of suspected measles see Figure (19).



Distribution of measles cases by week of onset, Shabwah governorate, February–May 2018

Figure (19): The surveillance officer in Shabwa governorate reported an increased number of suspected measles.

On May 24, 2018, a team from Yemen-Field Epidemiology Training Program was sent to investigate.

A total of 73 suspected cases were found. Almost 53% were from Habban district, 63% were males and 56% were among age group < 5 years. The overall AR was 82/100,000 population. Measles was significantly associated with contact with case (aOR = 27.3, 95% CI:1.3–551.7), malnourished children aged 6–60 months (aOR = 24.9, 95% CI:1.9–329.6) and unvaccinated children (aOR = 17.2, 95% CI:2.9–100.7). The six collected blood samples found to be positive for measles IgM84.

United Nations agencies have also highlighted the severe increase in vaccine-preventable diseases in Yemen, pointing out that the country recorded more than 22,000 measles cases in 2022, including 161 deaths. In April of this year, there had already been 16,114 cases. With diphtheria and pertussis – whooping cough – cases are also on the rise, as are deaths from each disease. ^[85]

The weekly epidemiological suspected measles in south and eastern governorate up to almost 3,674 with fatality rate 0.93% (see Figure 20).^[86]

Summary report of suspected measles cases and related death per each governorate



from W1 to W10 / 2023

Governorate	New reports Cases/Death in last two weeks					Cumulative reports			
	Week 9		Week 10		Difference reports status in last two weeks	Cases	Death	CFR	Attack Rate*10 ⁵
	Cases	Death	Cases	Death					
Albyan / أبين	72	2	9	1	▼	535	6	1	87.0
Aden / عدن	102	0	45	0	▼	617	1	0	61.9
Al Bayda / البيضاء	21	0	2	0	▼	57	1	2	7.4
Al Dhale'e / الضالع	43	0	6	0	▼	210	0	0	26.9
Al Hudaydah / الحديدة	26	0	7	0	▼	190	9	0	6.4
Al Mahrah / المهرة	26	1	7	0	▼	94	2	2	55.5
Hadramaut(AI-Mukalla) / حضرموت(المكلا)	14	0	8	0	▼	207	0	0	25.4
Hadramaut(Say'un) / حضرموت(سبوتن)	33	0	14	0	▼	533	2	0	76.7
Ibb / إب	80	0	14	0	▼	417	0	0	39.4
Marib / مأرب	18	0	0	0	▼	130	0	0	26.2
Shabwah / شبوة	25	0	16	0	▼	213	3	1	32.0
Socatra / سقطرى	0	0	0	0	►	0	0	0	0.0
Taiz / تعز	90	0	20	1	▼	470	10	2	15.3
Out of free governorate	0	0	0	0	►	1	0	0	0.01
Grand Total	570	3	148	2	-422	3674	34	0.93	27.9

Source: Measles surveillance line list, eIDEWS program, MOPHP/Aden

Note: All data analysis according to date of onset

Prepared by surveillance team, Aden

Figure (20): Summary report of suspected measles cases and related death per each governorate

2.6 COMPARISON BETWEEN MEASLES AND RUBELLA.

What is Measles?

Measles is a very contagious disease that is caused by an RNA virus, known as a paramyxovirus. The virus can stay alive for up to two hours in the air. Incubation of the disease is from 1 to 2 weeks but symptoms can last for up to 10 days.

It is most contagious during the early symptoms (prodromal stage) of the disease and the person remains contagious for quite some time. About 90% of people exposed will become ill with the measles.

People are infected when they come into contact with droplets produced by sick people who are coughing or sneezing.^[87]



Figure (21): *Measles Rash*

What is Rubella?

Rubella is caused by a virus which also has RNA as its nucleic acid. Similar to measles, it can be transmitted by respiratory secretions, from people coughing or sneezing.

People who are infected are contagious for up to a week before they show symptoms and for about two weeks after the symptoms develop.

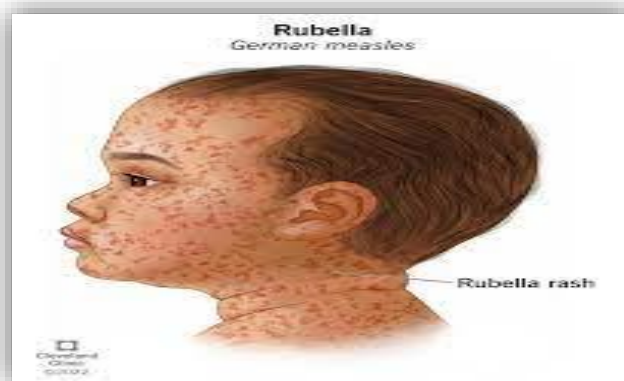


Figure (22): *Rubella rash*

People who are infected are contagious for up to a week before they show symptoms and for about two weeks after the symptoms develop.

It is also known as German measles and is not as contagious as measles. Many people who are exposed to rubella do not become ill. It is also not a severe illness except in those with a compromised immune system.

Incubation of the disease can take from about 2 to 3 weeks. Symptoms can include a low fever (less than 38.3° C), general feeling of discomfort, conjunctivitis and swollen lymph nodes. Painful joints can also occur in some people.

Painful swollen lymph nodes in the neck are common and the back of the throat becomes reddish in color.

No early symptoms (a prodromal stage), occurs in rubella. Rubella has some similar symptoms to measles in that there are a rash and a fever.

A rash first forms on the face then spreads to the rest of the body. It does not last long and starts to fade to tiny spots by the second day, at which time the fever stops. The rash can last up to 5 days.

Bruises that form on the soft palate of the mouth (known as Forchheimer spots), will join together to form a reddish area.

Rubella in a pregnant woman is very dangerous and can cause defects in a newborn such as deafness, microcephaly and even stillbirths. It can even lead to cataracts and heart defects in the newborn if the mother is exposed during pregnancy.

The best protection against rubella is the MMR vaccine. The incidence of rubella decreased after vaccination programs started.^[87]

The Epidemiological Situation of German Measles in Yemen:

The incidence rate of German measles in Yemen is generally high, reaching approximately 50.5 cases per million populations (more than 1,300 cases) in 2014, whereas this rate was 30 cases per million populations in 2013. It is observed that the incidence rate of German measles has increased in 2013 and 2014 due to improved surveillance of the disease. In this context, the Ministry of Health established a special surveillance system for congenital rubella syndrome to assess the disease burden and the impact of the vaccine that was introduced as part of routine immunization activities in February 2015.^[64]

Measles and rubella are leading causes of death, disease, and economic burden globally.

In 1980, before widespread global use of measles vaccine, an estimated 2.6 million measles deaths occurred worldwide. While much progress has been made, including more than 56 million measles-related deaths prevented through vaccination from 2000 – 2021, measles still claimed the lives of almost 130,000 people (mostly children) in 2021.

In 2021, the estimated number of measles cases was 9.5 million. The health consequences of measles and rubella infection can be lifelong, including economic losses for individuals, families and societies.

The last major rubella pandemic in 1962-1965 included an estimated 12.5 million infections and negatively affected 33,350 pregnancies in the United States. The development of a rubella vaccine reduced infections by as much as 78% 3 years after introduction. Seventy percent of all infants worldwide have access to the rubella vaccine. As of February 2022, almost 50 percent of countries have eliminated rubella and congenital rubella syndrome, but 19 countries have not started using the rubella vaccine.^[88]

In 2020 and 2021, reported measles cases and deaths were lower than most previous years. Measures to mitigate COVID-19, such as social distancing and mask use, may have helped prevent spread of measles and rubella viruses. Surveillance for measles and rubella has also declined, which impacts the timely detection of cases and outbreaks. Disruptive measles outbreaks were still reported and cases may have been underreported.^[88]

Measles and rubella can cause serious illness, birth defects, and death.

Measles and rubella (also known as “German measles”) are diseases that can lead to serious health complications, or even death. In unvaccinated pregnant women, rubella can lead to miscarriage, stillbirth or multiple birth defects that together are called congenital rubella syndrome (CRS).^[88]

Health problems caused by these diseases overlap. Each of them can cause brain damage, deafness, and blindness. Measles can cause pneumonia and diarrhea, while rubella and congenital rubella syndrome can lead to heart disorders.^[88]

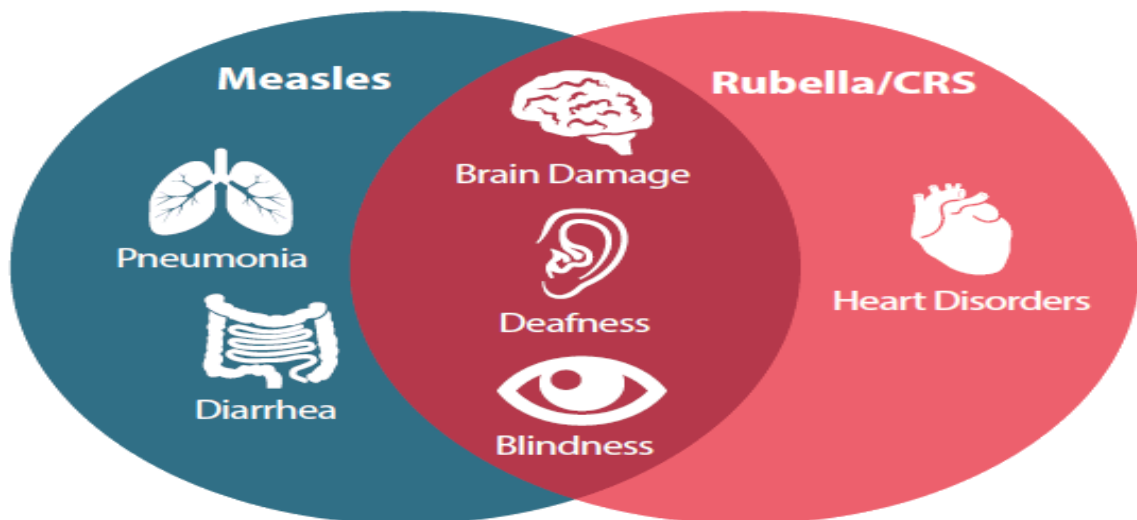


Figure (23): Health problems possible from measles and rubella / congenital rubella syndrome (CRS) overlap. ^[89]

What is the difference between Measles and Rubella?

- Measles is far more contagious and severe an illness than rubella.
- In measles there is a prodromal stage while there is no prodromal stage in Rubella.
- Incubation in measles is from 1 to 2 weeks, in rubella it is from 2 to 3 weeks.
- Symptoms of measles can last for up to 10 days, while symptoms of rubella usually last a maximum of 5 days.
- Swollen lymph nodes always occur with rubella but not often with measles.
- (Koplik's spots) are a sign in measles, while (Forschheimer spots) are a sign in rubella.
- Photophobia occurs in measles, but does not occur in rubella.
- In measles the fever can be as high as 40°C; rubella fever tends to be lower than 38.3°
- The measles rash consists of blotches which last a while, while the rubella rash consists of spots, which fades fast. ^[87]

2.7 LAST STATISTICS IN YEMEN REGARDING VACCINATION

Introduction:

In Yemen, efforts have been made to increase vaccination coverage and control outbreaks of measles. The country has faced challenges due to ongoing conflict and limited healthcare infrastructure, which have impacted the accessibility and delivery of vaccines. However, various organizations such as UNICEF, WHO, and local health authorities are working together to ensure that children receive their vaccinations.

It's important for parents and caregivers in Yemen to ensure that their children receive the recommended doses of the measles vaccine. Vaccination not only protects individuals from contracting measles but also helps prevent its spread within communities.

The historical milestones of the Expanded Immunization Program in Yemen:

- Before 1970: No vaccines were available.
- In 1977, the Expanded Immunization Program was established, providing vaccines that included six doses for children: polio (three doses), DTP (diphtheria, tetanus, pertussis) (three doses), BCG (Bacillus Calmette-Guérin) for tuberculosis (one dose), and measles (one dose).
- In 1998, the introduction of vitamin A supplementation was implemented.
- In 2004, the second dose of the measles vaccine was adopted for children at the age of 18 months.
- In September 2015, the introduction of the measles and rubella injection vaccine was implemented.
- In 2022, the booster dose of the measles and rubella vaccine, along with vitamin A, was adopted at school entry age.^[90]

Yemen Measles Immunization Rate:

According to the World Health Organization (WHO), based on 2021 statistics (Figure 24), the percentage of Children ages 12-23 months with measles immunization was 71 %. For that indicator, we provide data for Yemen from 1980 to 2021. The average value for Yemen during that period was 51 percent with a minimum of 2 percent in 1980 and a maximum of 74 percent in 1999. The latest value from 2021 is 71 percent. For comparison, the world average in 2021 based on 187 countries is 83 percent. See the global rankings for that indicator or use the country comparator to compare trends over time^[92].

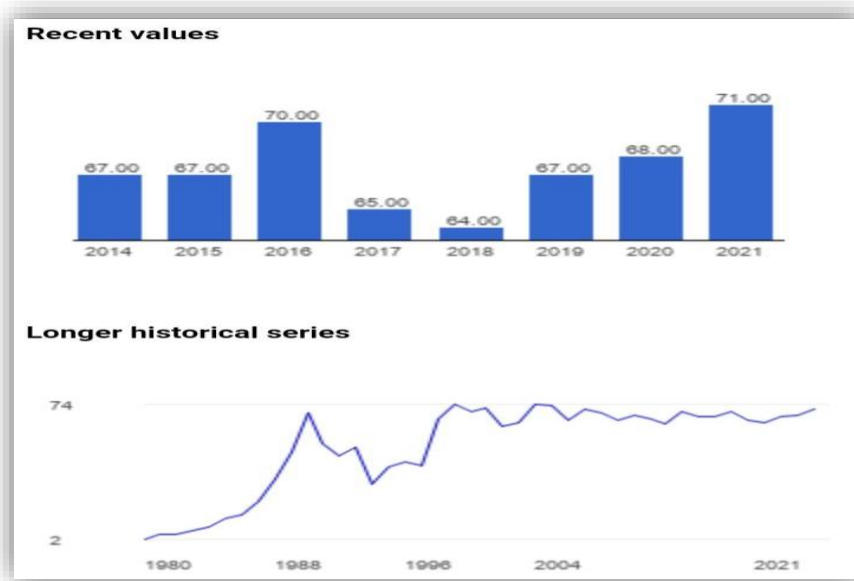


Figure (24): Measles Immunization rate 1980-2021

Cross-sector indicators:

Geographic area: Yemen.

Indicator: Percentage of children who received the 2nd dose of measles-containing vaccine, as per administered in the national schedule.

Unit of measure: % (Units).^[93]

WHO concerned over increase in measles and rubella cases among children in Yemen 31 August 2023—The World Health Organization (WHO) is concerned over increasing cases of measles and rubella among children in Yemen. As of 31 July this year, the number of suspected cases of measles and rubella in Yemen has reached almost 34,300 cases and 413 deaths, compared to 27,000 cases and 220 associated deaths in 2022. There is also limited information on the outbreak's impact on pregnant women who remain at high risk.

“Ideally, the outbreak response vaccination campaign should target at least all children under the age of ten to be comprehensive and effective; however, the current funding gap has eroded support and limited the target to children under five years of age the group with higher mortality rates,” said Dr Arturo Pesigan, WHO Representative in Yemen.

The increase in measles and rubella cases among children in Yemen this year is occurring within a context of economic decline and low incomes, displacement, and overcrowded living conditions

in camps, coupled with an overwhelmed health system, low immunization rates, and a large number of children who remain unreachable through routine immunization interventions. According to the WHO-UNICEF National Immunization Coverage Estimate for 2022, 27 percent of children under one year of age in Yemen are unvaccinated for measles and rubella and have not met the minimal set of vaccines for full protection.

WHO is working with the Yemeni Ministry of Public Health and Population (MoPHP) and partners to increase support for routine vaccination interventions. WHO also continues to work within the National Health Framework to provide technical and financial support to improve coverage among children? In 2022, WHO supported the protection of around 913,000 children from measles and rubella. As of July 2023, MoPHP with the support of WHO and other partners reached a coverage rate of around 65 percent of all children—both doses of measles and rubella (MR1 and MR2). A measles-rubella vaccination campaign, targeting 1.2 million children under the age of five, is planned to be implemented in September this year.^[94]

Protecting Yemeni children against measles:

WHO together with public health authorities and partners is implementing a vaccination campaign against outbreaks of measles and rubella. The campaign aims to protect 1.35 million infants and children up to age 10, in 74 high-risk districts of 10 governorates across Southern Yemen.



Figure (25): *Vaccination of Yemeni child*

Neama Hareb is a health worker at Khormaksar polyclinic in Aden. Since 4 June, she has been walking from house to house immunizing infants and children against measles and rubella. Neama

considers her work to be a race against the clock, as a fresh outbreak of the two vaccine preventable diseases has taken 30 young lives to date in Southern Yemen.

Neama's admits that the community immunization campaign is challenged by widely circulating false rumors that the vaccine is harmful to children.

“We are educating community members about the importance of taking the vaccine, and we are seeing an increase in the numbers of children being immunized,” said Ms. Hareb. “Encouraging mothers to get their children vaccinated can result in saving their lives, so this is very meaningful work”.

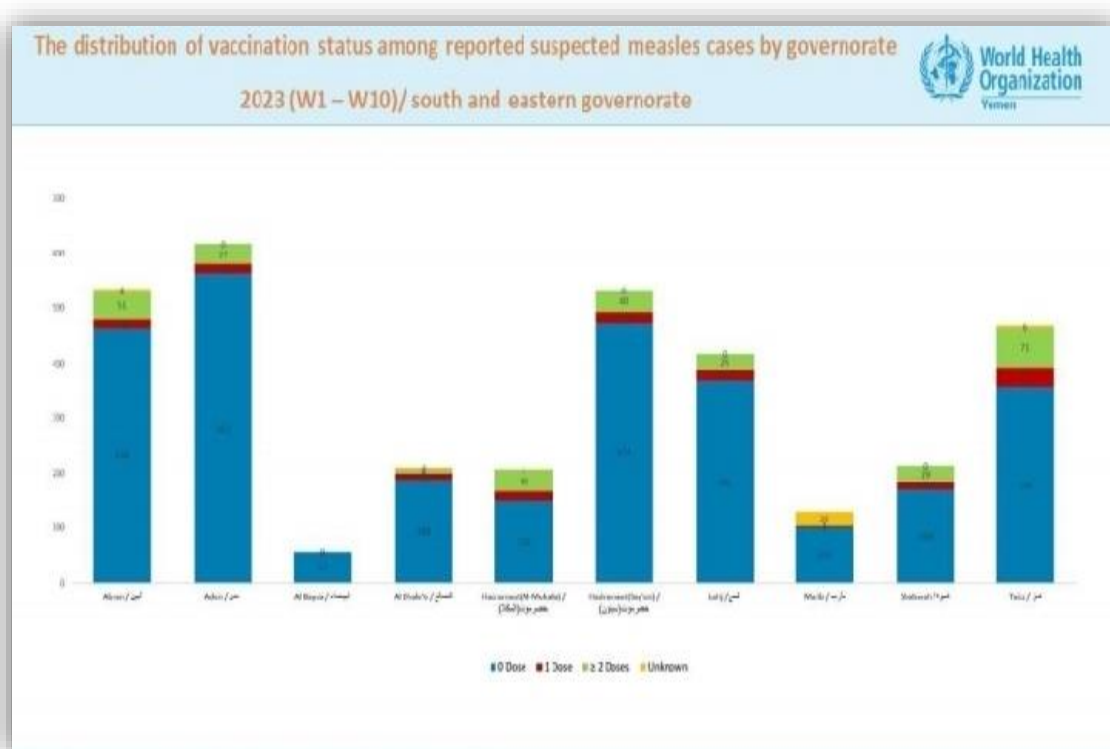


Figure (26): Distribution of vaccination status among reported suspected measles cases by governorate 2023

More than 1.2 million children from 6 months to 9 years have been vaccinated since the start of this campaign.

Measles ranks among the leading cause of death among young children despite availability of safe vaccines killing over 568 people daily in 2019 alone, mostly children. About 30% of children affected with congenital rubella syndrome die. Both diseases are highly contagious, and can cause serious health problems including brain damage, blindness and deafness, in non-fatal cases.

“One person with measles can infect 12-18 people, making it the most infectious -- yet vaccine preventable disease,” said WHO-Yemen Representative Dr. Adham Ismail Abdel Moneim. “Safe and effective vaccines to prevent measles and rubella have been available for over 50 years, and saved more than 31 million lives worldwide between 2000-2020”.

WHO is committed to helping Yemen detect, respond to, and lessen the harm of measles and rubella outbreaks,” Dr Abdel Moneim said. “The continued vital support of our partners has made this campaign possible -to prevent many more deaths from these two entirely preventable diseases”.

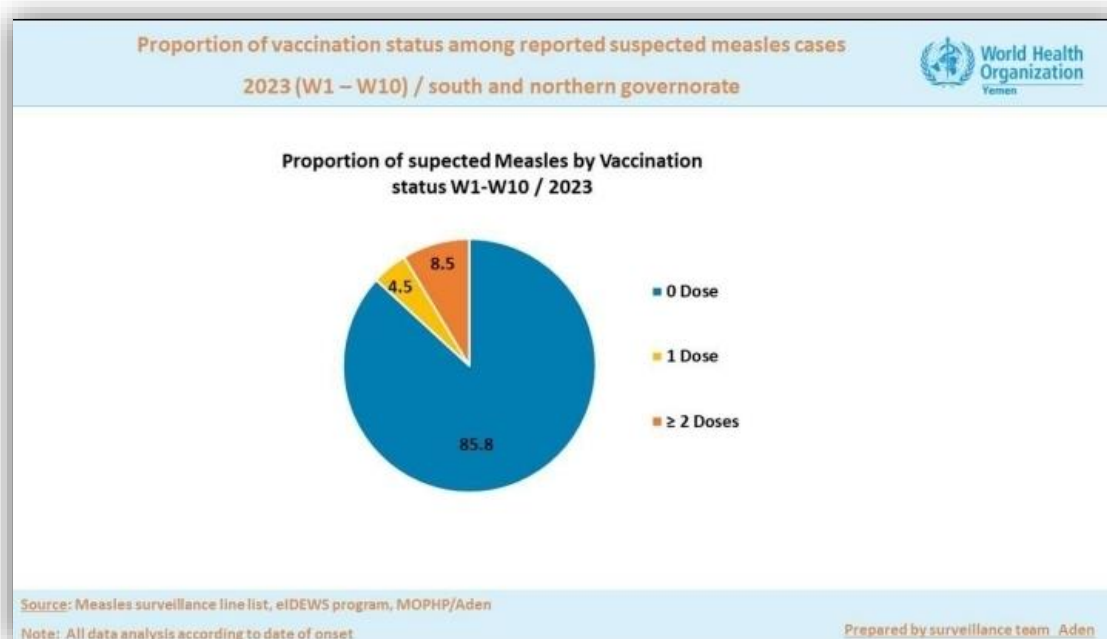


Figure (27): *Proportion of vaccination status reported suspected measles cases 2023.*

WHO is undertaking the measles-rubella outbreak vaccination campaign together with public health authorities, UNICEF, the World Bank International Development Association, the Government of Germany, and Measles-Rubella Initiative (MRI). Following closely on the heels of this campaign, WHO is launching the third round of an oral polio vaccine campaign that began in February and has so far immunized more than 2.2 million children up to age 5 against the vaccine-derived poliovirus (cVDPV2).^[95]

CHAPTER 3

CONCLUSION

To conclude, measles is one of the most contagious potentially fatal but vaccine preventable disease caused by measles virus and affect human leading to a widespread outbreak.

Fever and maculopapular rash, and at least one of cough, coryza, or conjunctivitis, are the main clinical symptoms in measles that appears early in the disease. Severe respiratory, neurological complications may occur especially among malnourished people, children under five of years, immunocompromised people, pregnant women.

Cases management are largely supportive, there is no specific antiviral therapy for the treatment of measles, and disease control largely depends on prevention. Despite the availability of a safe and effective vaccine, measles is still endemic in many countries and causes considerable morbidity and mortality, especially among children in resource-poor settings.

In Yemen, prevalence of measles is very high especially in the last few years. Despite many vaccination campaigns that have been carried out by the ministry of health, the disease still one of the most susceptible cause of death in the country.

CHAPTER 4

RECOMMENDATIONS

Recommendations

- 1- We recommend the Ministry of Health to conduct an expanded information campaign to aware the people about the risk of measles and encourage them to take the vaccines.
- 2- Urgent vaccination campaign especially for homes and remote villages to provide wide coverage for remote areas.
- 3- Ensure rapid detection of measles cases, through establishing primary medical centers in the areas far from the center of the governorates.
- 4- Ministry of Health should make the information more available and organized for research as we found difficulties in collecting national information.
- 5- Community members can help to support the vaccination campaigns by participating in outreach efforts, spreading the word about the importance of vaccines, and providing logistical support when and where needed.
- 6- Community members can help increase awareness about the importance of vaccinations by sharing accurate information about measles and vaccines and addressing common misconceptions.

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